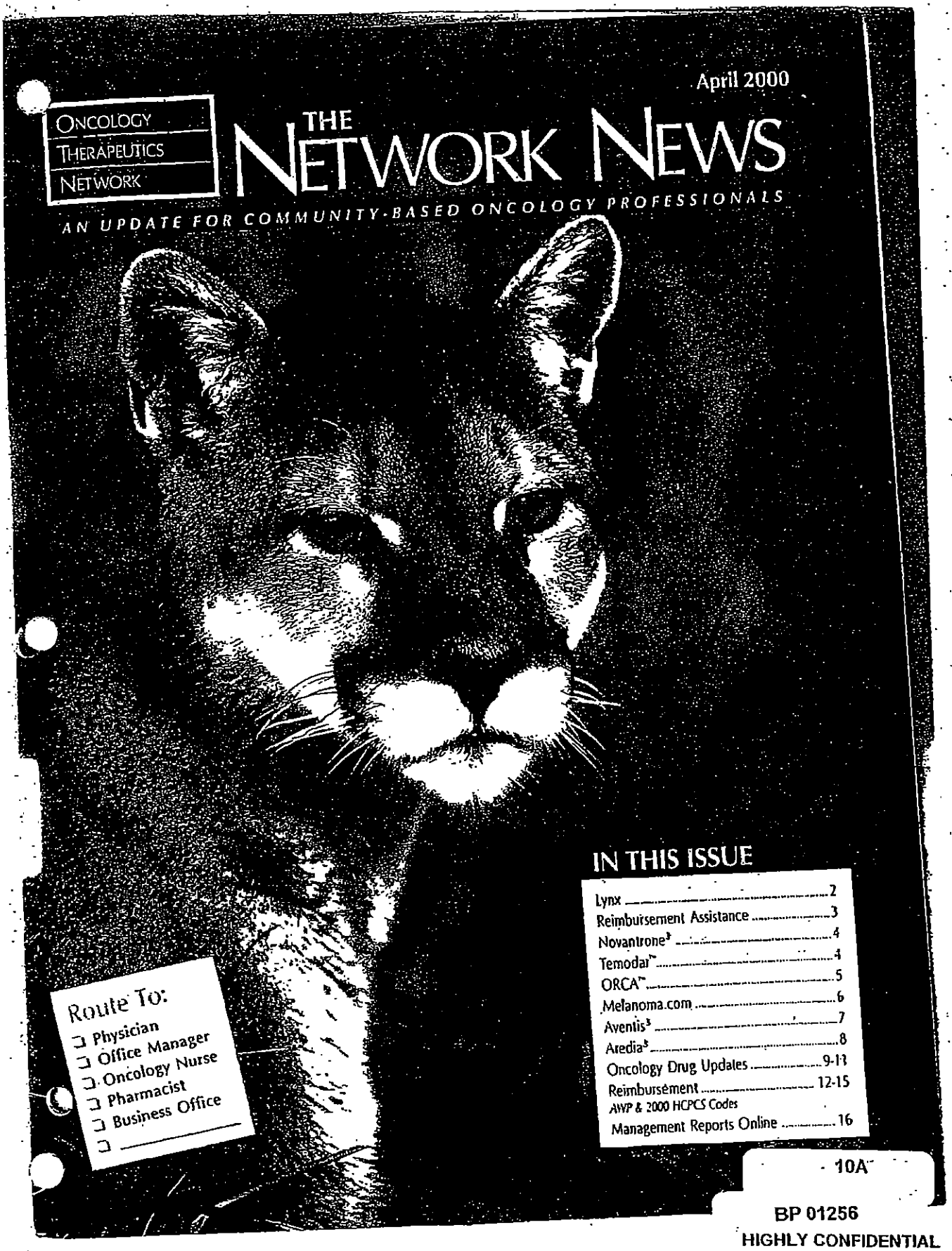
April 2000

ONCOLOGY THERAPEUTICS NETWORK

THE NETWORK NEWS

AN UPDATE FOR COMMUNITY-BASED ONCOLOGY PROFESSIONALS



Route To:
- ☐ Physician
- ☐ Office Manager
- ☐ Oncology Nurse
- ☐ Pharmacist
- ☐ Business Office
- ☐ _____

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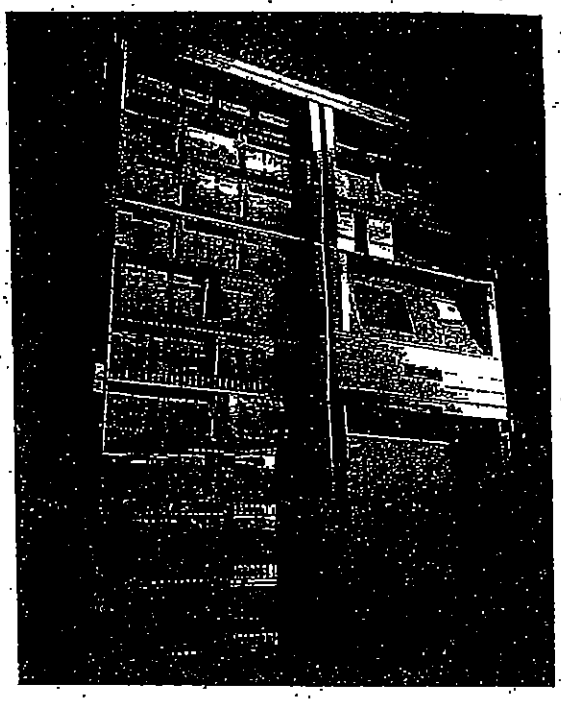
ONCOLOGY THERAPEUTICS NETWORK

Lynx™

- Controls Inventory
- Captures Lost Revenue
- Powerfully Manages Information



The Gold Standard

- ✓ Developed specifically for office-based oncology practices
- ✓ OTN has over four years experience installing and supporting Lynx
- ✓ Reference sites nationwide
- ✓ Proven scheduling and billing interfaces with common oncology practice software
- ✓ Comprehensive training program
- ✓ Ongoing technical support 24 hours a day, 7 days a week

Lynx Saves Time and Money

- ✓ Nationwide field support guaranteed to respond in less than four hours
- ✓ Extensive data collection and management resources
- ✓ Behind every Lynx system stands a dedicated OTN support team, including pharmacists and oncology nurses
- ✓ Automated inventory management of all products
- ✓ Reduces Inventory
- ✓ Captures lost billing charges

Over 350 oncology offices nationwide use the Lynx system

Call your OTN representative today to find out how to put the power of Lynx to work for your practice: 1-800-482-6700

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BP 01257

ONCOLOGY THERAPEUTICS NETWORK

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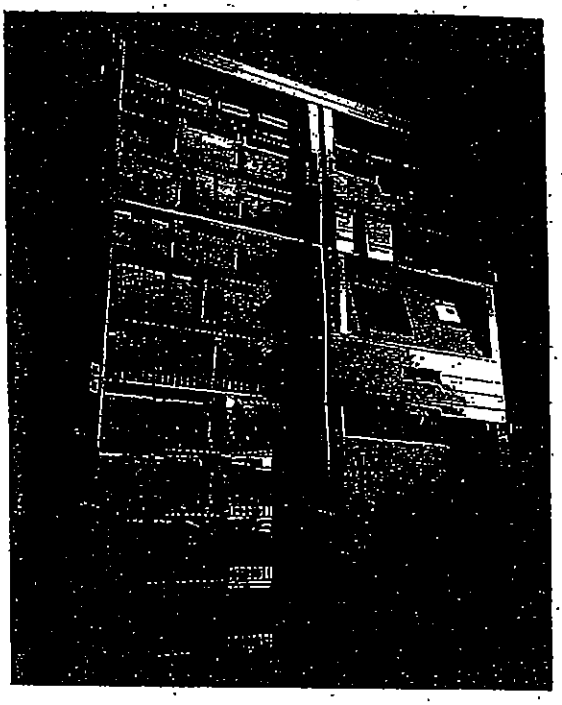

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REIMBURSEMENT ASSISTANCE

Bobbi Buell, MBA
President, Documedics

ONCOLOGY THERAPEUTICS NETWORK

Regulations Impact Cancer Practices

Balanced Budget Refinement Act (BBRA) of 1999

The BBRA changed Medicare payment for hospitals and, to some extent, for cancer care physicians. Highlights include:

Ambulatory Payment Classifications (APCs)

This proposed methodology for the hospital outpatient prospective payment system, is very harsh for hospital-based cancer clinics in that cancer drug payments will be limited to 556-216 without additional payments for supportive care drugs that accompany cancer therapy like anti-emetics, growth factors, biologics, etc. Technological changes would happen slowly, meaning that new cancer therapies would be paid at 556 for 2-3 years. The situation improved with BBRA – but it is pertinent to read the 'fine print.' Implementation of APCs is set to begin 7/1/2000.

- There will be an outlier payment. An outlier 'pool' will be made available for certain services, consisting of 2.5-3.0% of the total payments projected for outpatient hospital services. This pool will be used for services that have costs exceeding an unspecified threshold. Payment can be applied to any APC-paid service that exceeds the outlier threshold, and will be made on the hospital's aggregate cost-to-charge ratio.
- There will be a pass-through for certain types of drugs. For drugs that are covered by Medicare in a hospital outpatient setting, Medicare will make additional payments if they meet certain criteria: they must be Orphan drugs, cancer therapy which includes chemo, anti-emetics, hematopoietic growth factors, colony stimulating factors, biological response modifiers, a biphosphonate, and/or a device used in brachytherapy; or they must be radiopharmaceuticals. In addition, the pass-through will also apply to ANY drug or device that was not reimbursed by Medicare as of 12/31/96. *The payment for drugs will be the difference between the APC payment and 95% of AWP.* This provision is only good for 2-3 years. The amount of payments shall not exceed 2.5% of the total outpatient payments and, if the outlay exceeds HCFA projections, the pass-through can be reduced.
- Chemo AND chemo administration will be paid in another pass-through. In separate section, BBRA states that certain codes will be paid as if they were on the Part B (Physician) fee schedule. The chemo drug codes involved are J9000-J9020; J9040-J9151; J9170-J9185; J9200-J9201; J9206-J9208; J9211; J9230-J9245; and, J9265-J9600. Chemo administration codes include 36260-36262; 36489; 36640; 36823; and, 96405-96542. This pass-through does not seem to be as limited as the one for all drugs. How it's going to be paid (cost report versus claim) however, is still an issue.
- Temporary increase in hospice payments. For 2001, there will be a 0.5% increase and for 2002, there will be a 0.75% increase. These will NOT be built into the payment base.
- IVIG to undergo scrutiny. Medicare will undertake a study to determine whether IVIG (intravenous immune globulin) should be paid outside the hospital or office setting, and will investigate whether this can be done safely.
- There is now a transitional cushion against possible blows of APCs. For cancer hospitals ONLY, if the amount under APCs is different from pre-BBRA amounts, Medicare will pay the difference. This will not happen on a per claim basis – so there can still be cash flow ramifications to this. For other hospitals, there will be transitional payments of diminishing amounts through 2003.
- Physician update. The changes in the update factor to the physician fee schedule will be 'normalized' to guard against wild swings in payment. Changes to the Medicare fee schedule will be published by 11/1.
- More data to be collected on practice expense. Practice expense relative values for chemo administration have been inadequate for oncologists. This is because the payment is inadequate for amount of cost involved. Medicare is going to look at data provided by other entities to evaluate the fairness of practice expense relative values for all specialties.
- There will be a GAO study on safe and effective outpatient cancer therapy. The GAO will examine how cancer services should be paid in terms of practice expense relative values, work relative values, and standards for 'safe' treatment.
- Increase in PAP smear reimbursements. The rate will go up to $14.60.
- Transplant patients will get extended coverage for immunosuppressive drugs. Transplant patients whose drug benefit runs out in the next five years will get an extension of benefits. In 2000-2001, this extension will be eight months.

Medicare Physician Fee Schedule (MPFS)

Published in the *Federal Register*, Nov. 2, 1999, and effective 1/1/2000, the MPFS is also available online at www.HCFA.gov. Provisions include:

- Resource-based Malpractice Relative Values. Malpractice is one of the three relative value sets that determine Medicare payment. Since they are relatively insignificant in medical specialties, this does not have much influence on oncology payments.
- Conversion Factor. Important for negotiations with all insurance companies, for 2000, it will be $36.6137. This up from $34.7315 for 1999 – a 5.4% increase.
- Practice Expense Relative Values in Facilities. Facilities are hospitals (inpatient and outpatient), psych hospitals, ASCs, rehab hospitals and nursing homes. When physicians do professional services in these facilities that they ordinarily perform in their offices, they will take a reduction in Practice Expense RVUs. The important ones for physicians are outpatient EM services (99211-99215 and 99241-99245). Some of these reductions are 30-35%.
- Nurse Practitioner (NP) Qualifications. NPs can obtain a provider number and bill Medicare. Last year, Medicare proposed that NPs had to have a Masters' Degree to get a provider number. This was met with a storm of protest. Now, NPs without Masters' can be grandfathered until 1/1/2003. NPs should get provider numbers now.
- Coverage of Prostate Screening Tests for Men over 50 years old. Effective 1/1/00, men over 50 can have prostate screenings annually, if they are Medicare beneficiaries. The screening code is G0103. A provision is that Digital Rectal Exam (DRE) is also covered once a year; but, it is NOT payable with an EM service. It has the same value as 99211 and the code is G0102.
- A4550. A4550 is still around for use with bone marrows, lumbar punctures, thoracentesis, paracentesis, and intra-body chemos. The price is down to about $18.00.

Self Administration

HCFA stated last year that it would issue a policy regarding drugs that are administered intramuscularly and/or subcutaneously in the office. This policy could have meant the end of reimbursement for these types of cancer and supportive drugs. As part of the Omnibus Budget Reconciliation Act of 1999 (11/29/99), this policy will not be enacted for one year. In the interim, Medicare and Congress will hold two town meetings to ascertain what policy should be written. ■

NOTE: APCs [illegible]

ONCOLOGY THERAPEUTICS NETWORK

Novantrone®

(mitoxantrone for injection concentrate)
From Immunex Corporation

NOVANTRONE
MITOXANTRONE
For Injection Concentrate

Novantrone, in combination with corticosteroids, is indicated for initial cancer chemotherapy for the treatment of patients with pain related to advanced hormone-refractory prostate cancer.

Product Information

CATALOG NUMBER	NDC	ITEM	UNIT SIZE	ORDER QTY	PRICE/ UNIT*	AWP
902-200	58406-0640-03	Novantrone (2 mg/mL)	20 mg MDV	1	$759.00	$812.74
902-210	58406-0640-05	Novantrone (2 mg/mL)	25 mg MDV	1	$947.50	$1,015.90
902-220	58406-0640-07	Novantrone (2 mg/mL)	30 mg MDV	1	$1,138.00	$1,219.10

Novantrone Product Support:

Novantrone Reimbursement Hotline 1-800-321-4669
Medical Information 1-800-466-8639
J Code ..... J9293 per 5 mg
ICD-9 Code (HRPC) 185

Visit the website!
www.immunex.com

There's Still Hope

Schering

Temodar™
temozolomide
capsules

Largest Trial Conducted in Recurrent Anaplastic Astrocytoma

- Worldwide multicenter, single-arm trial at 32 centers (15 U.S., 17 International)
- 162 patients with anaplastic astrocytoma at first relapse
- Karnofsky Performance status ≥ 70
- Failed prior radiation therapy ± chemotherapy with a nitrosourea
- 54 out of 162 were considered chemotherapy refractory (relapsed following a procarbazine/nitrosourea therapy

22% of Refractory Patients Achieved A Response...

- 9% (5/54) were complete responders (CRs), 13% (7/54) were partial responders (PRs)
- Median duration for all responders: 50 weeks (16-114 weeks)
- Median duration for CRs: 64 (52-114 weeks)

...with Measurable Survival Results...*

- 45% of patients were progression-free at 6 months
- Median Progression-free-survival was 4.4 months
- 74% of patients were alive at 6 months
- Median overall survival was 15.9 months

* The indication for TEMODAR™ is based on the response rate in the indicated population. No results are available from randomized controlled trials in recurrent AA that demonstrate a clinical benefit resulting from treatment, such as improvement in disease-related symptoms, delayed disease progression, or improved survival.

ONCOLOGY THERAPEUTICS NETWORK

A Program Supporting the Reimbursement of Oral Chemotherapy and Supportive Care Medicines in Physician Offices

ORCA™

An Introduction to ORCA

ORCA (Oral Reimbursement for Cancer Agents) is a free service provided by Oncology Therapeutics Network (OTN), which can simplify and expedite billing and reimbursement for oral chemotherapy and supportive care medicines in your office.*

Why participate?

- Simplifies the use of oral therapies in the physician's office
- Eliminates concerns over reimbursement delays and denials
- Service is provided "free of charge" by OTN

How does ORCA work?

There are four components to the program:

1. Enrollment in the National Supplier Clearinghouse (NSC)
2. Drug fulfillment through OTN
3. Billing, collection, and appeals of individual claims through ORCA
4. Drug replacement is guaranteed if reimbursement is not approved

Which oral medications and insurance carriers are covered by ORCA?

- Cytoxan® Tablets (cyclophosphamide tablets, USP)
- VePesid® (etoposide) Capsules

The ORCA program covers all Medicare patients. It is expected that the program will be expanded in the near future to cover additional chemotherapeutic and supportive care medicines and additional insurance carriers.

Who is eligible to participate in ORCA?

Any office-based physician practice is eligible to participate in the ORCA program.

How do I enroll in the program?

1. If you are not already an OTN customer, call 1-800-482-6700 to set up an account.
2. Once you have set up an account, or if you are already an OTN customer, call the ORCA program at 1-877-SAY-ORCA (1-877-729-6722) to request an enrollment packet.

* The ORCA program is a free service provided by OTN and is administered by AccessMED, 6900 College Boulevard, Suite 1000, Overland Park, KS 66211. AccessMED is a leading reimbursement and consulting firm focused on oncology.

ONCOLOGY THERAPEUTICS NETWORK

www.melanoma.com

- Information about melanoma prevention, diagnosis, staging, and adjuvant therapy
- Skin self-examination techniques
- Skin safety, sun safety, and risk reduction
- Nutrition and exercise tips
- Resouce listings for melanoma patients, their families, and friends

LEADING THE WAY IN MELANOMA THERAPY AND SUPPORT

ONCOLOGY THERAPEUTICS NETWORK

Aventis®

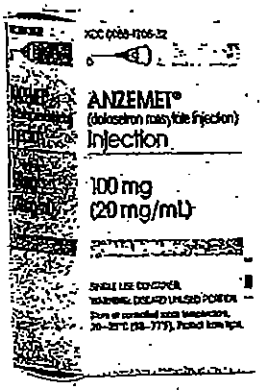
Aventis Pharmaceuticals
Kansas City, MO 64134

J-CODES
Injections: J1260, per 1 mg
Tablets: Q0180, per 100 mg

5-HT$_3$ Receptor Antagonist

Excellent Efficacy and Safety Profile

- Anzemet Injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin.
- Anzemet Tablets are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses.
- Proven Efficacy and Simplicity – Anzemet injection can be safely infused intravenously as rapidly as 100 mg/30 seconds or diluted in compatible IV solutions and infused over 15 minutes. The recommended oral dosage of Anzemet is 100 mg given within one hour before chemotherapy.



For more information on dosing and administration, please contact your Hoechst Marion Roussel representative.

Great Value!

CATALOG NUMBER	NDC	BRAND NAME	ITEM	UNIT SIZE	ORDER QUANTITY	PRICE/ UNIT	AWP
900-250	0088-1206-32	Anzemet	dolasetron mesylate	100 mg vial	1	$77.75	$155.88
970-300	0088-1203-05	Anzemet	dolasetron mesylate	100 mg tablets	5	$321.45	$343.20
970-305	0088-1203-29	Anzemet	dolasetron mesylate	100 mg tablets blister pack	5	$321.45	$686.40
970-310	0088-1203-43	Anzemet	dolasetron mesylate	100 mg tablets unit dose	10	$642.95	$686.40

Outstanding Support:

Reimbursement and Patient Assistance Program Hotline 1-888-895-2219

Call the Anzemet Hotline for help with reimbursement and patient assistance programs, Monday through Friday between 10 a.m. and 6 p.m. ET.

Call OTN today at 1-800-482-6700 to place your order!

Visit the website! www.anzemet.com

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ONCOLOGY THERAPEUTICS NETWORK

Novartis Oncology is pleased to introduce

Performance Program for Medical Practices

Highlights* †

2% discount at the time of order on AREDIA when you enroll in the program by purchasing through our direct selling agent, Oncology Therapeutics Network (OTN).

In addition, based on your AREDIA unit purchases through OTN, participants will be eligible to receive rebates of 3%, 4% or 5% depending on the growth in milligram purchases during the year 2000 compared to the year 1999.

3% rebate you achieve **an increase up to 10%** over your total 1999 AREDIA milligram purchases

4% rebate if you achieve **an increase >10% and ≤20%** over your total 1999 AREDIA milligram purchases

5% rebate if you achieve **an increase >20%** over your total 1999 AREDIA milligram purchases

To participate in this program, call OTN at 1-800-482-6700 or ask your Novartis Oncology Sales Specialist.

* This program applies only to office-based oncology and urology practices unless otherwise agreed by to Novartis.

† This pricing is subject to acceptance to terms and conditions contained in a price list to be made available through OTN.

NOVARTIS

ONCOLOGY

NOVARTIS PHARMACEUTICALS CORPORATION
EAST HANOVER, NEW JERSEY 07936

TAXOTERE (docetaxel)

BRIEF SUMMARY

WARNING

TAXOTERE (docetaxel for Injection Concentrate should be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

The incidence of treatment-related mortality associated with TAXOTERE therapy is increased in patients with abnormal liver function and in patients receiving higher doses (see WARNINGS).

TAXOTERE should generally not be given to patients with bilirubin > upper limit of normal (ULN), or to patients with SGOT and/or SGPT >1.5 x ULN concomitant with alkaline phosphatase > 2.5 x ULN. Patients with alterations of bilirubin or abnormalities of transaminase component with alkaline phosphatase are at increased risk for the development of grade 4 neutropenia, febrile neutropenia, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity, and toxic death. Patients with isolated elevations of transaminase > 1.5 x ULN alone had a higher rate of hepatic toxic deaths grade 4 but did not have an increased incidence of toxic death. Bilirubin, SGOT or SGPT and alkaline phosphatase values should be obtained prior to each cycle of TAXOTERE therapy and reviewed by the treating physician.

TAXOTERE therapy should not be given to patients with neutrophil counts of < 1500 cells/mm³. In order to monitor the occurrence of neutropenia, which may be severe and result in infection, frequent blood cell counts should be performed on all patients receiving TAXOTERE.

Severe hypersensitivity reactions characterized by hypotension and/or bronchospasm, or generalized rash/erythema occurred in 2.2% (2/92) of patients who received the recommended 3-day dexamethasone premedication. Hypersensitivity reactions requiring discontinuation of the TAXOTERE infusion were reported in five patients who did not receive premedication. These reactions resolved after discontinuation of the infusion and the administration of appropriate therapy. TAXOTERE should not be given to patients who have a history of severe hypersensitivity reactions to DAXOTERE or to other drugs formulated with polysorbate 80 (see WARNINGS).

Severe fluid retention occurred in 6.5% (6/92) of patients despite use of a 3-day dexamethasone premedication regimen. It was characterized by one or more of the following events: poorly tolerated peripheral edema, generalized edema, pleural effusion requiring urgent drainage, dyspnea at rest, cardiac tamponade, or pronounced abdominal distention prior to scheduled dose (see PRECAUTIONS).

INDICATIONS AND USAGE

TAXOTERE (docetaxel) for Injection Concentrate is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.

CONTRAINDICATIONS

TAXOTERE is contraindicated in patients who have a history of severe hypersensitivity reactions to docetaxel or to other drugs formulated with polysorbate 80.

TAXOTERE should not be used in patients with neutrophil counts of < 1500 cells/mm³.

WARNINGS

TAXOTERE (docetaxel) for Injection Concentrate should be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

Toxic Deaths: TAXOTERE administered at 100 mg/m² was associated with deaths considered possibly or probably related to treatment in 2.9% (19/660) of metastatic breast cancer patients, both previously treated and untreated, with normal baseline liver function and in 11.5% (7/61) of patients with various tumor types who had abnormal baseline liver function (SGOT and/or SGPT > 1.5 times ULN together with AP > 2.5 times ULN). Among patients dosed at 60 mg/m², mortality related to treatment occurred in 0.6% (3/480) of patients with normal liver function, and in 3 of 7 patients with abnormal liver function. Approximately half of these deaths occurred during the first cycle. Sepsis accounted for the majority of the deaths.

Premedication Regimens: All patients should be premedicated with oral corticosteroids, such as dexamethasone 16 mg per day (e.g., 8 mg BID) for 3 days starting 1 day prior to TAXOTERE to reduce the severity of fluid retention and hypersensitivity reactions (see DOSAGE AND ADMINISTRATION section). This regimen was evaluated in 92 patients with metastatic breast cancer previously treated with chemotherapy given TAXOTERE at a dose of 100 mg/m² every 3 weeks.

Hypersensitivity Reactions: Patients should be observed closely for hypersensitivity reactions, especially during the first and second infusions. Severe hypersensitivity reactions characterized by hypotension and/or bronchospasm, or generalized rash/erythema occurred in 2.2% of the 92 patients premedicated with 3-day corticosteroids. Hypersensitivity reactions requiring discontinuation of the TAXOTERE infusion were reported in 5 out of 1750 patients with various tumor types who did not receive premedication, but in 0/92 patients premedicated with 3-day corticosteroids. Patients with a history of severe hypersensitivity reactions should not be rechallenged with TAXOTERE.

Hematologic Effects: Neutropenia (< 2000 neutrophils/mm³) occurs in virtually all patients given 60-100 mg/m² of TAXOTERE and grade 4 neutropenia (< 500 cells/mm³) occurs in 85% of patients given 100 mg/m² and 75% of patients given 60 mg/m². Frequent monitoring of blood counts is, therefore, essential so that dose can be adjusted. TAXOTERE should not be administered to patients with neutrophils < 1500 cells/mm³.

Febrile neutropenia occurred in about 12% of patients given 100 mg/m² but was very uncommon in patients given 60 mg/m². Hematologic responses, febrile reactions and infections, and rates of septic death for different regimens are dose related and are described in CLINICAL STUDIES.

Thirty breast cancer patients with severe liver impairment (bilirubin > 1.7 times ULN) developed fatal gastrointestinal bleeding associated with severe drug-induced thrombocytopenia.

Hepatic Impairment: (see BOXED WARNING).

Fluid Retention: (see BOXED WARNING).

Pregnancy: TAXOTERE can cause fetal harm when administered to pregnant women. Studies in both rats and rabbits at doses 0.3 and 0.03 mg/kg/day, respectively (about ¼ and ¼₀ the daily maximum recommended human dose on a mg/m² basis), administered during the period of organogenesis, have shown that TAXOTERE is embryotoxic and fetotoxic (characterized by intrauterine mortality, increased resorption, reduced fetal weight, and fetal ossification delay). The doses indicated above also caused maternal toxicity.

There are no adequate and well-controlled studies in pregnant women using TAXOTERE. If TAXOTERE is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus or potential risk for loss of the pregnancy. Women of childbearing potential should be advised to avoid becoming pregnant during therapy with TAXOTERE.

PRECAUTIONS

General: Recording patients may not experience an improvement in performance status on therapy and may experience worsening. The relationship between changes in performance status, response to therapy, and treatment-related side effects has not been established.

Hematologic Effects: In order to monitor the occurrence of myelotoxicity, it is recommended that treatment peripheral blood cell counts be performed on all patients receiving TAXOTERE. Patients should not be retreated with subsequent cycles of TAXOTERE until neutrophils recover to a level > 1500 cells/mm³ and platelets recover to a level > 100,000 cells/mm³.

A 25% reduction in the dose of TAXOTERE is recommended during subsequent cycles following severe neutropenia (< 500 cells/mm³) lasting 7 days or more, febrile neutropenia, or a grade 4 infection in a TAXOTERE-(docetaxel) for Injection Concentrate cycle (see DOSAGE AND ADMINISTRATION section).

Hypersensitivity Reactions: Hypersensitivity reactions may occur within a few minutes following initiation of a TAXOTERE infusion. Minor reactions such as flushing or localized skin reactions occur, interruption of therapy is not required. More severe reactions, however, require the immediate discontinuation of TAXOTERE and appropriate therapy. All patients should be premedicated with an oral corticosteroid prior to the initiation of the infusion of TAXOTERE (see BOXED WARNING and WARNINGS: Premedication Regimens).

Cutaneous: Localized erythema of the extremities with edema followed by

desquamation has been observed. In case of severe skin toxicity, an adjustment in dosage is recommended (see DOSAGE AND ADMINISTRATION section). The discontinuation rate due to skin toxicity was 1.6% (15/965) for metastatic breast cancer patients. Among 92 breast cancer patients premedicated with 3-day corticosteroids, there were no cases of severe skin toxicity reported and no patient discontinued TAXOTERE due to skin toxicity.

Fluid Retention: Severe fluid retention has been reported following TAXOTERE therapy (see BOXED WARNING and WARNINGS: Premedication Regimen). Patients should be premedicated with oral corticosteroids prior to each TAXOTERE administration to reduce the incidence and severity of fluid retention (see DOSAGE AND ADMINISTRATION section). Patients with pre-existing effusions should be closely monitored from the first dose for the possible exacerbation of the effusions. When fluid retention occurs, peripheral edema usually starts in the lower extremities and may become generalized with a median weight gain of 2 kg.

Among 92 breast cancer patients premedicated with 3-day corticosteroids, moderate fluid retention occurred in 27.2% and severe fluid retention in 6.5%. The median cumulative dose to onset of moderate or severe fluid retention was 819 mg/m². 9.8% (9/92) of patients discontinued treatment due to fluid retention: 4 patients discontinued with severe fluid retention; the remaining 5 had mild or moderate fluid retention. The median cumulative dose to treatment discontinuation due to fluid retention was 1021 mg/m². Fluid retention was completely, but sometimes slowly, reversible with a median of 16 weeks from the last infusion of TAXOTERE to resolution (range: 0 to 42+ weeks). Patients developing peripheral edema may be treated with standard measures, e.g., salt restriction, oral diuretic(s).

Neurologic: Severe neurosensory symptoms (paresthesia, dysesthesia, pain) were observed in 5.5% (53/965) of metastatic breast cancer patients, and resulted in treatment discontinuation in 6.1%. When these symptoms occur, dosage must be adjusted. If symptoms persist, treatment should be discontinued (see DOSAGE AND ADMINISTRATION section). Patients who experienced neurotoxicity in clinical trials and for whom follow-up information on the complete resolution of the event was available had spontaneous reversal of symptoms with a median of 9 weeks from onset (range: 0 to 106 weeks). Severe peripheral motor neuropathy mainly manifested as distal extremity weakness occurred in 4.4% (42/965).

Asthenia: Severe asthenia has been reported in 14.9% (144/965) of metastatic breast cancer patients but has led to treatment discontinuation in only 1.8%. Symptoms of fatigue and weakness may last a few days up to several weeks and may be associated with deterioration of performance status in patients with progressive disease.

Information for Patients: For additional information, see the accompanying Patient Information Leaflet.

Drug Interactions: There have been no formal clinical studies to evaluate the drug interactions of TAXOTERE with other medications. In vitro studies have shown that the metabolism of docetaxel may be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 3A4, such as cyclosporine, terfenadine, ketoconazole, erythromycin, and troleandomycin. Caution should be exercised with these drugs when treating patients receiving TAXOTERE as there is a potential for a significant interaction.

Carcinogenicity, Mutagenicity, Impairment of Fertility: No studies have been conducted to assess the carcinogenic potential of TAXOTERE. TAXOTERE has been shown to be clastogenic in the in vitro chromosome aberration test in CHO-K1 cells and in the in vivo micronucleus test in the mouse, but it did not induce mutagenicity in the Ames test or the CHO/HGPRT gene mutation assays. TAXOTERE produced no impairment of fertility in rats when administered in multiple IV doses of up to 0.3 mg/kg (about 1/50 the recommended human dose on a mg/m² basis), but decreased testicular weights were reported. This correlates with findings of a 10-cycle toxicity study (dosing once every 21 days for 6 months) in rats and dogs in which testicular atrophy or degeneration was observed at IV doses of 5 mg/kg in rats and 0.375 mg/kg in dogs (about 1/3 and 1/15 the recommended human dose on a mg/m² basis, respectively). An increased frequency of dosing in rats produced similar effects at lower dose levels.

Pregnancy: Pregnancy Category D (see WARNINGS section).

Nursing Mothers: It is not known whether TAXOTERE is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from TAXOTERE, mothers should discontinue nursing prior to taking the drug.

Pediatric Use: The safety and effectiveness of TAXOTERE in pediatric patients have not been established.

ADVERSE REACTIONS

Adverse drug reactions occurring in at least 5% of patients are compared for three populations who received TAXOTERE administered at 100 mg/m² as a 1-hour infusion every 3 weeks: 2045 patients with various tumor types and normal baseline liver function tests; the subset of 965 patients with locally advanced or metastatic breast cancer, both previously treated and untreated with chemotherapy, who had normal baseline liver function tests; and an additional 61 patients with various tumor types who had abnormal liver function tests at baseline. These reactions were considered possibly or probably related to TAXOTERE. At least 95% of these patients did not receive hematopoietic support. The safety profile is generally similar in patients receiving TAXOTERE for the treatment of breast carcinoma and in patients with other tumor types.

Summary of Adverse Events in Patients Receiving TAXOTERE at 100 mg/m²

Adverse Event	All Tumor Types Normal LFTs* n=2045 %	All Tumor Types Elevated LFTs** n=61 %	Breast Cancer Normal LFTs* n=965 %
Hematologic			
Neutropenia			
<2000 cells/mm³	95.5	96.7	98.5
<500 cells/mm³	75.4	88.5	85.9
Leukopenia			
<4000 cells/mm³	95.6	98.3	98.6
<1000 cells/mm³	31.6	46.7	43.7
Thrombocytopenia			
<100,000 cells/mm³	8.0	24.6	9.2
Anemia			
<11 g/dL	90.4	91.8	93.6
<8 g/dL	8.8	31.1	7.7
Febrile Neutropenia***	11.0	26.2	12.3

Summary of Adverse Events in Patients Receiving TAXOTERE at 100 mg/m² (cont'd)

Adverse Event	All Tumor Types Normal LFTs* n=2045 %	All Tumor Types Elevated LFTs** n=61 %	Breast Cancer Normal LFTs* n=965 %
Septic Death	1.6	4.9	1.4
Non-Septic Death	0.8	6.6	0.5
Infections			
Any	21.6	32.8	22.2
Severe	6.1	16.4	6.4
Fever in Absence of Infection			
Any	31.2	41.0	35.1
Severe	2.1	8.2	2.2
Hypersensitivity Reactions Regardless of Premedication			
Any	21.0	19.7	17.6
Severe	4.2	9.8	2.5
With 3-day Premedication	n=92	n=3	n=92
Any	15.2	33.3	15.2
Severe	2.2	0	2.2
Fluid Retention Regardless of Premedication			
Any	47.0	39.3	59.7
Severe	6.9	8.2	8.9
With 3-day Premedication	n=92	n=3	n=92
Any	64.1	66.7	64.1
Severe	6.5	33.3	6.5
Neurosensory			
Any	49.3	34.4	58.3
Severe	4.3	0	5.5
Cutaneous			
Any	47.6	54.1	47.0
Severe	4.8	9.8	5.2
Nail Changes			
Any	30.6	23.0	40.5
Severe	2.5	4.9	3.7
Gastrointestinal			
Nausea	38.9	37.7	42.1
Vomiting	22.3	23.0	23.4
Diarrhea	38.7	32.8	42.6
Severe	4.7	4.9	5.5
Stomatitis			
Any	41.7	49.2	51.7
Severe	5.5	13.0	7.4
Alopecia	75.8	62.3	74.2
Asthenia			
Any	61.8	52.5	66.3
Severe	12.8	24.6	14.9
Myalgia			
Any	18.9	16.4	21.1
Severe	1.5	1.6	1.8
Arthralgia	9.2	6.6	8.2
Infusion Site Reactions	4.0	3.3	4.0

*Normal Baseline LFTs: Transaminases ≤ 1.5 times ULN or alkaline phosphatase ≤ 2.5 times ULN or isolated elevations of transaminases or alkaline phosphatase up to 5 times ULN

**Elevated Baseline LFTs: SGOT and/or SGPT > 1.5 times ULN concurrent with alkaline phosphatase > 2.5 times ULN

***Febrile Neutropenia: ANC grade 4 with fever > 38°C with IV antibiotics and/or hospitalization

Hematologic (see WARNINGS): Reversible marrow suppression was the major dose-limiting toxicity of TAXOTERE. The median time to nadir was 7 days, while the median duration of severe neutropenia (<500 cells/mm³) was 7 days. Among 2045 patients with solid tumors and normal baseline LFTs, severe neutropenia occurred in 75.4% and lasted for more than 7 days in 2.9% of cycles.

Febrile neutropenia (<500 cells/mm³ with fever > 38°C with IV antibiotics and/or hospitalization) occurred in 11% of patients with solid tumors, in 12.3% of patients with metastatic breast cancer, and in 9.8% of 92 breast cancer patients premedicated with 3-day corticosteroids.

Severe infectious episodes occurred in 6.1% of patients with solid tumors, in 6.4% of patients with metastatic breast cancer, and in 5.4% of 92 breast cancer patients premedicated with 3-day corticosteroids.

Thrombocytopenia (<100,000 cells/mm³) associated with fatal gastrointestinal hemorrhage has been reported.

Hypersensitivity Reactions: Severe hypersensitivity reactions are discussed in the BOXED WARNING, WARNINGS, and PRECAUTIONS sections. Minor events, including flushing, rash with or without pruritus, chest tightness, back pain, dyspnea, drug fever, or chills, have been reported and resolved after discontinuing the infusion and appropriate therapy.

Fluid Retention: (see BOXED WARNING, WARNINGS: Premedication Regimen, and PRECAUTIONS sections).

Cutaneous: Severe skin toxicity is discussed in PRECAUTIONS. Reversible cutaneous reactions characterized by a rash including localized eruptions, mainly on the feet and/or hands, but also on the arms, face, or thorax, usually associated with pruritus, have been observed. Eruptions generally occurred within 1 week after TAXOTERE infusion, recovered before the next infusion, and were not disabling.

Severe nail disorders were characterized by hypo- or hyperpigmentation, and occasionally by onycholysis (in 0.8% of patients with solid tumors) and pain.

Neurologic (see PRECAUTIONS).

Gastrointestinal: Gastrointestinal reactions (nausea and/or vomiting and/or diarrhea) were generally mild to moderate. Severe reactions occurred in 3-5% of patients with solid tumors and to a similar extent among metastatic breast cancer patients. The incidence of severe reactions was 1% or less for the 92 breast cancer patients premedicated with 3-day corticosteroids.

Severe stomatitis occurred in 5.5% of patients with solid tumors, in 7.4% of patients with metastatic breast cancer, and in 1.1% of the 92 breast cancer patients premedicated with 3-day corticosteroids.

Cardiovascular: Hypotension occurred in 2.8% of patients with solid tumors; 1.2% required treatment. Clinically meaningful events such as heart failure, sinus tachycardia, atrial flutter, dysrhythmia, unstable angina, pulmonary edema, and hypertension occurred rarely. 8.1% (7/86) of metastatic breast cancer patients receiving TAXOTERE 100 mg/m² in a randomized trial and who had serial left ventricular ejection fractions assessed developed deterioration of LVEF by ≥ 10% associated with a drop below the institutional lower limit of normal.

Infusion Site Reactions: Infusion site reactions were generally mild and consisted of hyperpigmentation, inflammation, redness or dryness of the skin, phlebitis, extravasation, or swelling of the vein.

Hepatic: In patients with normal LFTs at baseline, bilirubin values greater than the ULN occurred in 8.9% of patients. Increases in SGOT or SGPT > 1.5 times the ULN, or alkaline phosphatase > 2.5 times ULN, were observed in 18.9% and 7.3% of patients, respectively. While on TAXOTERE, increases in SGOT and/or SGPT > 1.5 times ULN concomitant with alkaline phosphatase > 2.5 times ULN occurred in 4.3% of patients with normal LFTs at baseline. (Whether these changes were related to the drug or underlying disease has not been established.)

Ongoing Evaluation: The following serious adverse events of uncertain relationship to TAXOTERE have been reported:

Body as a whole: abdominal pain, diffuse pain, chest pain, radiation recall phenomenon

Cardiovascular: atrial fibrillation, deep vein thrombosis, ECG abnormalities, thrombophlebitis, pulmonary embolism, syncope, tachycardia, myocardial infarction

Digestive: constipation, duodenal ulcer, esophagitis, gastrointestinal hemorrhage, intestinal obstruction, ileus, gastrointestinal perforation, neutropenic enterocolitis, dehydration in relation to digestive disorders

Nervous: confusion, seizures

Respiratory: dyspnea, acute pulmonary edema, acute respiratory distress syndrome, interstitial pneumonia

Urogenital: renal insufficiency

OVERDOSAGE

There is no known antidote for TAXOTERE overdosage. In case of overdosage, the patient should be kept in a specialized unit where vital functions can be closely monitored. Anticipated complications of overdosage include: bone marrow suppression, peripheral neurotoxicity, and mucositis.

There were two reports of overdose. One patient received 150 mg/m² and the other received 200 mg/m² as 1-hour infusions. Both patients experienced severe neutropenia, mild asthenia, cutaneous reactions, and mild paresthesia, and recovered without incident.

In mice, lethality was observed following single IV doses that were ≥ 154 mg/kg (about 4.5 times the recommended human dose on a mg/m² basis); neurotoxicity associated with paralysis, non-extension of hind limbs, and myelin degeneration was observed in mice at 48 mg/kg (about 1.5 times the recommended human dose on a mg/m² basis). In male and female rats, lethality was observed at a dose of 20 mg/kg (comparable to the recommended human dose on a mg/m² basis) and was associated with abnormal mitosis and necrosis of multiple organs.

DOSAGE AND ADMINISTRATION

The recommended dose of TAXOTERE is 60-100 mg/m² administered intravenously over 1 hour every 3 weeks.

Premedication Regimen: All patients should be premedicated with oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg BID) for 3 days starting 1 day prior to TAXOTERE administration in order to reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions (see BOXED WARNING, WARNINGS, and PRECAUTIONS sections).

Rx only

Please see product circular for complete prescribing information.

RHÔNE-POULENC RORER PHARMACEUTICALS INC.
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ONCOLOGY DRUG UPDATES

ONCOLOGY THERAPEUTICS NETWORK

Update on the Diagnosis and Treatment of Prostate Cancer

Barry R. Goldspiel, PharmD, FASHP

Prostate cancer is the most common cancer among American men and is the second leading cause of cancer-related deaths in all males. In the year 2000, 180,400 new cases and 31,900 deaths are expected.[1] Because of advances in diagnostic techniques, such as prostate-specific antigen (PSA) testing and greater public awareness, the majority of cases are now diagnosed when the cancer is still localized. This has resulted in reduced mortality and a decrease in the number of patients who present with advanced disease. In recent years, research has focused on strategies for improving localized disease control. Recent studies suggest that neoadjuvant androgen deprivation before radiation or surgery for localized or locally advanced prostate cancer may produce improved outcomes.

While androgen deprivation is still considered standard therapy for the initial treatment of metastatic prostate cancer, the best method to induce androgen deprivation – orchiectomy, a luteinizing hormone-releasing hormone (LH-RH) analog, or the combination of either with an antiandrogen – is still controversial. New approaches, including a renewed interest in chemotherapy and a reevaluation of clinical end points are being used for patients with advanced prostate cancer. This article will discuss PSA testing; localized management with neoadjuvant androgen deprivation, combined androgen blockade for metastatic prostate cancer, and chemotherapy regimens in advanced prostate cancer management.

Prostate-Specific Antigen Testing

PSA has good prostate specificity and is a very useful tumor marker.[2,3] Unfortunately, benign conditions, such as prostatitis, urinary retention, and benign prostatic hypertrophy can also elevate PSA levels. To increase PSA specificity, several indices have been developed,[2,3] including PSA density, age-related PSA levels, volume-referenced PSA, and percent free PSA. Of these indices, volume-referenced PSA and percent free PSA seem to be the most useful.[3] Volume-referenced PSA controls for gland volume (which usually increases with age) and creates a separate acceptable PSA range for gland size ranges. Unbound or free PSA represents a minor portion of the total circulating PSA, and free PSA is lower in men with prostate cancer than in those with benign prostatic hypertrophy. For men with total PSA levels from 4.1 to 10 ng/mL (suspicious for prostate cancer), the lower limit for normal free PSA ranges from 17% to 25%.[3] In men with lower PSA levels (2.5 to 4 ng/mL), where detecting cancer might greatly improve survival, free PSA levels < 25% suggest prostate cancer.[3] Another new test, ProstAsure®, simultaneously analyzes total PSA levels, prostate acid phosphatase, and creatinine phosphokinase enzymes in relation to age. In comparative studies, ProstAsure® performed better than analyses for free PSA levels alone and was effective in detecting cancer in patients with a total PSA level less than 4 ng/mL.[3] PSA testing, clinical stage, and Gleason score is also used to predict whether the prostate cancer is organ-confined at diagnosis.[4]

Prostate Cancer Treatment

Androgen deprivation, used in the past only for advanced prostate cancer, now has a role for patients with localized prostate cancer. Also, using clinical benefit as an acceptable response for patients with advanced prostate cancer has caused a renewed interest in testing various chemotherapy agents and combinations in this prostate cancer patient population.

Neoadjuvant Androgen Deprivation for Localized Prostate Cancer

As more patients are diagnosed with localized prostate cancer, new strategies are being developed to improve outcomes in these patients. Messing et al[5] demonstrated that immediate hormonal therapy to induce androgen deprivation (ie, with an LH-RH analog or orchiectomy) improved survival and reduced the recurrence risk in patients with node-positive prostate cancer.

Neoadjuvant androgen-ablative therapy has also been used to reduce tumor size or "downstage" disease prior to definitive radical prostatectomy or radiation therapy in patients with stage B2 or C prostate cancer.[5-8] The improved outcomes associated with neoadjuvant androgen deprivation include decreased local progression rate after radiation therapy, decreased positive surgical margin rate, decreased radiation-related toxicity to surrounding normal tissue, and increased probability of finding organ-confined disease at surgery.[6-8] Flutamide (Eulexin®) (in combination with an LH-RH agonist) and goserelin (Zoladex®) (in combination

Continued on next page

with flutamide) are FDA-approved for use prior to and during the period of radiation therapy for patients with stage B2 or C prostate cancer.

While it is believed that neoadjuvant androgen-ablative therapy reduces tumor volume, making the radiation therapy or surgery more effective, it is possible that the duration of androgen deprivation may also contribute to the improved outcome. Bolla et al[9] demonstrated that goserelin, given during and continued for three years after definitive radiotherapy, compared to radiation therapy alone improved local control and survival in patients with locally advanced prostate cancer. Thus, while androgen deprivation seems useful in localized prostate cancer, which androgen deprivation therapy (orchiectomy, an LH-RH analog, or the combination of either with an antiandrogen) and the optimal duration of neoadjuvant/adjuvant therapy still needs to be defined.[8]

Androgen Deprivation for Advanced Prostate Cancer

Androgen-ablative therapies for patients with metastatic prostate cancer include orchiectomy or administering an LH-RH agonist, either alone or in combination with an antiandrogen (ie, combined androgen blockade [CAB]). Initial studies comparing CAB to orchiectomy or an LH-RH agonist alone seemed promising; however, several well-designed, randomized trials have demonstrated no consistent benefit with CAB.[10-13] Three meta-analyses of trials comparing CAB to conventional medical or surgical castration have been performed (Table 1).[14-16] These meta-analyses failed to demonstrate a clear advantage of CAB. Some studies where CAB proved more beneficial than monotherapy showed that the response difference was most pronounced in patients with minimal disease (ie, no disease in ribs, long bones, or soft tissue other than lymph nodes) and a good performance status; however, this benefit is not consistent either.[17]

There is still controversy about when to start patients with advanced prostate cancer on androgen deprivation.[17,18] Only one randomized trial has addressed this issue and this trial favored starting androgen deprivation at time of diagnosis.[19] However, this practice has not been completely adopted because of several questions about the trial design.

It is not clear which combinations of therapy to use in this patient population. There are two LH-RH agonists currently available in long-acting depot formulations. All of the antiandrogens (eg, flutamide, bicalutamide, nilutamide) share similar FDA-approved indications; flutamide and bicalutamide are indicated in combination with an LH-RH agonist and nilutamide is indicated in combination with orchiectomy.[18] Adverse effects common to all antiandrogens include gynecomastia, breast tenderness, hot flushes, diarrhea, and liver function test abnormalities.[18] Only one randomized comparison of two antiandrogens (flutamide and bicalutamide) has been conducted; diarrhea was more common in the flutamide-treated patients than in the bicalutamide-treated patients.[13] Antiandrogen-withdrawal syndromes, where patients have responded with significant PSA reductions and improved clinical symptoms when the antiandrogen is discontinued, have been described for all three antiandrogens.[20,21]

Information thus far suggests that we might not be using CAB optimally.[17,18,22] Strategies where intermittent androgen deprivation have been described,[22] and are based on prolonging the response to androgen deprivation therapy by reducing the possibility for developing androgen independence. These strategies include using CAB around the time of LH-RH therapy initiation to reduce the symptoms from the flare phenomenon and using PSA as a marker for when to stop and start androgen deprivation therapy.

Chemotherapy for Advanced Prostate Cancer

While no antineoplastic agent or combination is known to prolong survival in patients with advanced prostate cancer, some agents or combinations do provide clinical benefit and/or reductions in a meaningful surrogate end point such as PSA level.[23,24] Clinical benefit includes improved quality of life, reduced pain, and reduced analgesic requirements.

Mitoxantrone combined with prednisone or hydrocortisone can produce a meaningful clinical benefit response.[25,26] Pain reduction, reduced analgesic requirements, and improved quality of life occur in around 30% of patients.[25] Several other single agents or combinations, such as estramustine plus vinblastine, estramustine plus etoposide, ketoconazole plus doxorubicin, estramustine plus paclitaxel, docetaxel, and etoposide plus cyclophosphamide can produce responses manifested as decreased PSA levels, pain relief, and delays in bone scan progression.[25]

There is a need to develop new agents for advanced prostate cancer that affect survival. Current investigations are exploring new molecular targets, such as apoptosis-inducing agents, differentiating agents, antimetastasis agents, vaccines, vitamin-D analogs, cyclin-dependent kinase inhibitors, monoclonal antibodies, growth receptor antibodies, and oncogene regulators.[23]

Continued on next page

ONCOLOGY THERAPEUTICS NETWORK

Continued from the previous page

Conclusions

More cases of prostate cancer are diagnosed when the cancer is localized, because better screening and diagnostic methods, such as the various PSA indices, have been developed. Localized prostate cancer is curable with surgery or radiation therapy. Androgen deprivation, as neoadjuvant or adjuvant therapy, can improve local disease control and survival. Androgen ablation can provide effective symptom palliation for patients with advanced prostate cancer. However, it is not clear if CAB using an antiandrogen with either orchiectomy or an LH-RH agonist is significantly better than either orchiectomy or an LH-RH agonist alone. Ongoing studies are attempting to define the best initial therapy, determine when to initiate therapy, identify which patient subpopulation might benefit most from a given treatment modality, and identify which surrogate markers should be used to monitor disease activity. For patients who become hormone-refractory, chemotherapy can provide clinical benefit manifested as pain reduction and reduced analgesic requirements. Continued efforts to develop new agents directed at prostate cancer-specific molecular targets may provide new therapeutic approaches that positively affect survival. ■

Table 1. *Meta-Analyses of Randomized Trials Comparing Combined Androgen Blockade to Androgen Deprivation Monotherapy*

14	21 trials 10 trials	7871	at 2 y: 0.97 at 5 y: 0.87	0.87–1.09 0.81–0.94
15	13 trials, including only nonsteroidal antiandrogens	3732	0.81	0.74–0.94
16	7 trials, comparing nilutamide plus orchiectomy to orchiectomy alone	1191	0.84	0.70–1.00

CAB=combined androgen blockade * A relative risk < 1 indicates that CAB reduces mortality

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Average Wholesale Prices and 2000 HCPCS Codes

The Average Wholesale Prices (AWPs) and HCPCS codes for drugs commonly used in cancer treatment are provided for your use as a reimbursement resource. Products are listed alphabetically by their generic name. The AWPs are obtained from the 2000 *Red Book* and the March 2000 *Red Book Update*. For drugs that have multiple manufacturers, the AWP for the product most commonly stocked by OTN is listed. For ease of use, we list the AWP information in the first three columns and the billing code and units in the next two columns. Please refer to the Sourcebook for a complete listing of HCPCS codes.

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Proleukin®						
Aldesleukin		53905-0991-01		J9015		800-775-7533
Ethyol®						
Amifostine		17314-7253-03		J0207		800-609-1083
Fungizone®						
Amphotericin B Oral Susp		00087-1162-10				800-872-8718
Blenoxane®						
Bleomycin Sulfate, pwd		00015-3010-20		J9040		800-872-8718
Bleomycin Sulfate, pwd		00015-3063-01		J9040		800-872-8718
Xeloda®						
Capecitabine 150mg Tablet		00004-1100-51		J8520		800-443-6676
Capecitabine 500mg Tablets		00004-1101-16		J8521		800-443-6676
Paraplatin®						
Carboplatin, pwd		00015-3213-30		J9045		800-872-8
Carboplatin, pwd		00015-3214-30		J9045		800-872-8
Carboplatin, pwd		00015-3215-30		J9045		800-872-8
BiCNU®						
Carmustine, pwd		00015-3012-38		J9050		800-872-8718
Platinol®-AQ						
Cisplatin 1mg/mL Inj		00015-3220-22		J9062		800-872-8718
Cisplatin 1mg/mL Inj		00015-3221-22		J9062		800-872-8718
Leustatin®						
Cladribine 1mg/mL Inj		59676-0201-01		J9065		800-553-3851
Cytogam®						
Cytomegalovirus Immune Globulin		60574-3301-01		J0850		
Cytoxan® Lyophilized						
Cyclophosphamide Lyopholized		00015-0539-41		J9093		800-872-8718
Cyclophosphamide Lyopholized		00015-0546-41		J9094		800-872-8718
Cyclophosphamide Lyopholized		00015-0547-41		J9095		800-872-8718
Cyclophosphamide Lyopholized		00015-0548-41		J9096		800-872-8718
Cyclophosphamide Lyopholized		00015-0549-41		J9097		800-872-8718
Cytoxan® Tablets						
Cyclophosphamide 25mg Tablet		00015-0504-01		J8530		800-872-8718
Cyclophosphamide 50mg Tablet		00015-0503-01		J8530		800-872-8718
Cyclophosphamide 50mg Tablet		00015-0503-02		J8530		800-872-8718
Cytarabine pwd		55390-0131-10		J9100		
Cytarabine pwd		55390-0132-10		J9110		
Cytarabine pwd		55390-0133-01		J9110		
Cytarabine pwd		55390-0134-01		J9110		
DTIC-Dome®						
Dacarbazine, pwd		00026-8151-20		J9140		800-998-9180
DaunoXome®						
Daunorubicin citrate liposome 2mg/ml inj		56146-0301-01		J9151		800-226-7056
Cerubidine®						
Daunorubicin HCl, pwd		55390-0281-10		J9150		
DDAVP®						
Desmopressin Acetate 4mcg/ml		00075-2451-01		J2597		610-454-8110
Zinecard®						
Dexrazoxane, pwd		00013-8715-62		J1190		800-808-9111
Dexrazoxane, pwd		00013-8725-89		J1190		800-808-9111
Diphenhydramine HCl 50mg/ml Inj		00641-0376-25		J1200		
Taxotere®						
Docetaxel 20mg/0.5ml, Inj		00075-8001-20		J9170		800-996-6626
Docetaxel 20mg/0.5ml		00075-8001-80		J9170		800-996-6626

REIMBURSEMENT

ONCOLOGY THERAPEUTICS NETWORK

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Anzemet®						
Dolasetron 20mg/ml inj	5 ml	00088-1206-32	155.88	J1260	10mg	800-221-4025
Rubex®						
Doxorubicin HCL pwd	50 mg	00015-3352-22	197.15	J9000	10mg	800-872-8718
Doxorubicin HCL pwd	100 mg	00015-3353-22	394.29	J9000	10mg	800-872-8718
Doxorubicin HCL pwd	10 mg	55390-0231-10	45.08	J9000	10mg	
Doxorubicin HCL pwd	20 mg	55390-0232-10	90.16	J9000	10mg	
Doxorubicin HCL pwd	50 mg	55390-0233-01	225.40	J9000	10mg	
Doxorubicin HCl 2mg/ml inj	5 ml	55390-0235-10	47.35	J9000	10mg	
Doxorubicin HCl 2mg/ml inj	10 ml	55390-0236-10	94.70	J9000	10mg	
Doxorubicin HCl 2mg/ml inj	25 ml	55390-0237-01	236.74	J9000	10mg	
Doxorubicin HCl 2mg/ml inj	100 ml	55390-0238-01	945.98	J9000	10mg	
Adriamycin™						
Doxorubicin RDF, pwd	10 mg	00013-1086-91	53.64	J9000	10mg	800-242-7014
Doxorubicin RDF, pwd	50 mg	00013-1106-79	268.18	J9000	10mg	800-242-7014
Doxorubicin RDF, pwd	150 mg	00013-1116-83	788.44	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml, inj	5 ml	00013-1136-91	56.34	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml	10 ml	00013-1146-91	112.66	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml	25 ml	00013-1156-79	281.68	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml	37.5 ml	00013-1176-87	422.51	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml	100 ml	00013-1166-83	1,104.13	J9000	[illegible]	800-242-7014
Doxil®						
Doxorubicin, HCL liposome 2mg/ml inj	10 ml	61471-0295-12	656.25	J9001	10mg	800-609-1082
Procrit®						
Epoetin Alpha 2000u/ml inj	1 ml	59676-0302-01	24.00	Q0136	1000units	800-553-3851
Epoetin Alpha 3000u/ml inj	1 ml	59676-0303-01	35.00	Q0136	1000units	800-553-3851
Epoetin Alpha 4000u/ml inj	1 ml	59676-0304-01	48.00	Q0136	[illegible]	800-553-3851
Epoetin Alpha 10, 000u/ml inj	1 ml	59676-0310-01	[illegible]	Q0136	[illegible]	800-553-3851
Epoetin Alpha 20, 000u/ml inj	1 ml	59676-0320-01	[illegible]	Q0136	[illegible]	800-553-3851
Epoetin Alpha 40, 000u/ml inj	1 ml	59676-0340-01	[illegible]	Q0136	[illegible]	800-553-3851
VePesid®						
Etoposide 50mg Capsule	20 caps	00015-3091-45	[illegible]	J8560	[illegible]	800-872-8718
Etoposide 20mg/ml, inj	5 ml	00015-3095-20	[illegible]	J9182	[illegible]	800-872-8718
Etoposide 20mg/ml, inj	7.5 ml	00015-3084-20	[illegible]	J9182	[illegible]	800-872-8718
Etoposide 20mg/ml, inj	25 ml	00015-3061-20	[illegible]	J9182	[illegible]	800-872-8718
Etoposide 20mg/ml, inj	50 ml	00015-3062-20	[illegible]	J9182	[illegible]	800-872-8718
Etopophos®						
Etoposide Phosphate, pwd	100 mg	00015-3404-20	124.14	J9182	[illegible]	800-872-8718
Fludara®						
Fludarabine Phosphate, pwd	50 mg	50419-0511-06	242.25	J9185	50mg	800-473-5832
Fluorouracil 50mg/ml, inj	10 ml	00013-1036-91	3.20	J9190	500mg	800-242-7014
Fluorouracil 50mg/ml, inj	50 ml	00013-1046-94	16.04	J9190	500mg	800-242-7014
Fluorouracil 50mg/ml, inj	100 ml	00013-1056-94	32.06	J9190	500mg	800-242-7014
Neupogen®						
Filgrastim(G-CSF) 300mcg/ml, inj	300 mcg	55513-0530-10	122.30	J1440	300mcg	800-272-9376
Filgrastim(G-CSF) 300mcg/ml, inj	480 mcg	55513-0546-10	[illegible]	J1441	480mcg	800-272-9376
Gemzar®						
Gemcitabine HCL pwd	200 mg	00002-7501-01	[illegible]	J9201	200mg	888-443-6927
Gemcitabine HCL pwd	1 Gram	00002-7502-01	[illegible]	J9201	200mg	888-443-6937
Leukine®						
Sargramostin(GM-CSF), pwd	250 mcg	58406-0002-33	[illegible]	J2820	[illegible]	800-321-4669
Sargramostin(GM-CSF) 500mcg/ml, inj	1 ml	58406-0050-30	288.59	J2820	[illegible]	800-321-4669
Zoladex®						
Goserelin Acetate, implant	3.6 mg syringe	00310-0960-36	[illegible]	J9202	[illegible]	800-400-4140
Goserelin Acetate, implant	10.8 mg syringe	00310-0961-30	[illegible]	J9202	[illegible]	800-400-4140
Kytril®						
Granisetron HCl 1mg/ml, inj	1 ml	00029-4149-01	195.20	J1626	[illegible]	800-699-3806
Granisetron HCl 1mg/ml, inj	4 ml	00029-4152-01	[illegible]	J1626	[illegible]	800-699-3806
Ifex®						
Ifosfamide pwd	1 Gram	00015-0556-41	[illegible]	J9208	[illegible]	800-872-8718
Ifosfamide pwd	3 Gram	00015-0557-41	[illegible]	J9208	[illegible]	800-872-8718
Ifex®/Mesnex™						
Ifosfamide(10x1g)/Mesna(10x1g MDV)	Combo-Pack	00015-3554-27	[illegible]	J9208/J9209	[illegible]	800-872-8718
Ifosfamide(2x3g)/Mesna(6x1g MDV)	Combo-Pack	00015-3564-15	[illegible]	J9208/J9209	[illegible]	800-872-8718
Ifosfamide(5x1g)/Mesna(3x1g MDV)	Combo-Pack	00015-3556-26	[illegible]	J9208/J9209	[illegible]	800-872-8718
Venoglobulin S						
Immune Globulin 50mg/ml, inj w/IV set	50 ml	49669-1612-01	[illegible]	J1561	[illegible]	
Immune Globulin 50mg/ml, inj w/IV set	100 ml	49669-1613-01	[illegible]	J1561	[illegible]	

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ONCOLOGY THERAPEUTICS NETWORK

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Immune Globulin 50mg/ml, inj w/IV set		49669-1614-01		J1561		
Immune Globulin 100mg/ml, inj w/IV set		49669-1622-01		J1561		
Immune Globulin 100mg/ml, inj w/IV set		49669-1623-01		J1561		
Immune Globulin 100mg/ml, inj w/IV set		49669-1624-01		J1561		
Immune Globulin 100mg/ml, inj		00026-0648-12		J1561		800-998-9180
Immune Globulin 100mg/ml, inj		00026-0648-20		J1561		800-998-9180
Immune Globulin 100mg/ml, inj		00026-0648-73		J1561		800-998-9180
Immune Globulin 100mg/ml, inj		00026-0648-24		J1561		800-998-9180
Immune Globulin, pwd		52769-0471-72		J1562		
Immune Globulin, pwd		52769-0471-75		J1562		
Immune Globulin, pwd		52769-0471-80		J1562		
RHO (d) Immune Globulin, pwd		60492-0021-01		J2792		
RHO (d) Immune Globulin, pwd		60492-0023-01		J2792		
RHO (d) Immune Globulin, pwd		60492-0024-01		J2792		
Intron® A						
Interferon Alpha 2B 3MIU/0.5ml		00085-1184-02		J9214		800-521-7157
Interferon Alpha 2B 5MIU/0.5ml		00085-1191-02		J9214		800-521-7157
Interferon Alpha 2B 10MIU/ML		00085-1179-02		J9214		800-521-7157
Interferon Alpha 2B 6MIU/ml, inj		00085-1168-01		J9214		800-521-7157
Interferon Alpha 2B 10MIU/ML, inj		00085-1133-01		J9214		800-521-7157
Interferon Alpha 2B, pwd		00085-0120-02		J9214		800-521-7157
Interferon Alpha 2B, pwd		00085-0571-02		J9214		800-521-7157
Interferon Alpha 2B, pwd		00085-1110-01		J9214		800-521-7157
Interferon Alpha 2B, pwd		00085-0285-02		J9214		800-521-7157
Interferon Alpha 2B, pwd		00085-0539-01		J9214		800-521-7157
Roferon® A						
Interferon Alpha 2A 3MIU/ML, inj		00004-2009-09		J9213		800-443-6676
Interferon Alpha 2A 6MIU/ml, inj		00004-2007-09		J9213		800-443-6676
Interferon Alpha 2A 9MIU/0.9ml, inj		00004-2010-09		J9213		800-443-6676
Interferon Alpha 2A 6MIU/ml, inj		00004-2011-09		J9213		800-443-6676
Interferon Alpha 2A 36MIU/ml, inj		00004-2012-09		J9213		800-443-6676
Camptosar®						
Irinotecan HCL 20mg/ml, inj		00009-7529-02		J9206		800-242-7014
Irinotecan HCL 20mg/ml, inj		00009-7529-01		J9206		800-242-7014
Leucovorin Calcium, pwd		55390-0051-10		J0640		
Leucovorin Calcium, pwd		55390-0052-10		J0640		
Leucovorin Calcium, pwd		55390-0053-01		J0640		
Leucovorin Calcium, pwd		58406-0623-07		J0640		800-321-4669
Lupron®						
Leuprolide Acetate, pwd		00300-3342-01		J9217		800-453-8438
Leuprolide Acetate, pwd		00300-3346-01		J9217		800-453-8438
Lorazepam 2mg/ml, inj		00008-0581-04		J2060		
Lorazepam 2mg/ml, inj		00008-0581-01		J2060		
Lorazepam 4mg/ml, inj		00008-0570-01		J2060		
Lorazepam 2mg/ml, inj		00008-0581-02		J2060		
Mannitol 25%, inj		00074-1031-01		J2150		
Mustargen®						
Mechlorethamine HCL, pwd		00006-7753-31		J9230		800-994-2111
Megace®						
Megestrol Acetate 20mg Tablet		00015-0595-01				800-872-8718
Megestrol Acetate 40mg Tablet		00015-0596-41				800-872-8718
Megestrol Acetate 40mg Tablet		00015-0596-46				800-872-8718
Megestrol Acetate 40mg Tablet		00015-0596-45				800-872-8718
Megestrol Acetate oral susp 40mg/ml		00015-0508-42				800-872-8718
Alkeran®						
Melphalan HCL, pwd		00173-0130-93		J9245		800-722-9294
Melphalan 2mg Tablet		00173-0045-55		J8600		800-722-9294
Mesnex™						
Mesna 100mg/ml, inj		00015-3563-02		J9209		800-872-8718
Methotrexate Sodium, pwd		58406-0673-01		J9250		800-321-4669
Methotrexate Sodium, pwd		58406-0671-05		J9260		800-321-4669
Methotrexate Sodium 25mg/ml, inj		55390-0031-10		J9260		
Methotrexate Sodium 25mg/ml, inj		55390-0032-10		J9260		
Methotrexate Sodium 25mg/ml, inj		55390-0033-10		J9260		
Methotrexate Sodium 25mg/ml, inj		55390-0034-10		J9260		
Methotrexate Sodium 25mg/ml, inj		58406-0681-14		J9260		800-321-4669
Methotrexate Sodium 25mg/ml, inj		58406-0681-17		J9260		800-321-4669
Methotrexate Sodium 2.5mg Tablet		00555-0572-02		J8610		

REIMBURSEMENT

ONCOLOGY THERAPEUTICS NETWORK

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Methotrexate Sodium 2.5mg Tablet		00555-0572-35		J8610		
Mutamycin®						
Mitomycin, pwd		00015-3001-20		J9280		800-872-8718
Mitomycin, pwd		00015-3002-20		J9290		800-872-8718
Mitomycin, pwd		00015-3059-20		J9291		800-872-8718
Novantrone®						
Mitoxantrone HCl 2mg/ml, inj	10 ml	58406-0640-03		J9293		800-321-4669
Mitoxantrone HCl 2mg/ml, inj	12.5 ml	58406-0640-05		J9293		800-321-4669
Mitoxantrone HCl 2mg/ml, inj	15 ml	58406-0640-07		J9293		800-321-4669
Sandostatin®						
Octreotide Acetate 50mcg/ml, inj	1 ml	00078-0180-03		J9999/J3490		800-257-3273
Octreotide Acetate 100mcg/ml, inj	1 ml	00078-0181-03		J9999/J3490		800-257-3273
Octreotide Acetate 500mcg/ml, inj	1 ml	00078-0182-03		J9999/J3490		800-257-3273
Sandostatin LAR® Depot						
Octreotide Acetate, pwd	10 mg	00078-0340-84		J2352		800-257-3273
Octreotide Acetate, pwd	20 mg	00078-0341-84		J2352		800-257-3273
Octreotide Acetate, pwd	30 mg	00078-0342-84		J2352		800-257-3273
Zofran®						
Ondansetron HCl 2mg/ml, inj	20 ml	00173-0442-00		J2405		800-745-2967
Ondansetron HCl 2mg/ml, inj	2 ml	00173-0442-02		J2405		800-745-2967
Ondansetron 32mg/50ml, premixed bag	50 ml	00173-0461-00		J2405		800-745-2967
Neumega®						
Oprelvekin, pwd	5 mg	58394-0004-01		J2355		888-638-6342
Taxol®						
Paclitaxel 6mg/ml, inj	30 mg	00015-3475-30		J9265		800-872-8718
Paclitaxel 6mg/ml, inj	100 mg	00015-3476-30		J9265		800-872-8718
Paclitaxel 6mg/ml, inj	300 mg	00015-3479-11		J9265		800-872-8718
Aredia®						
Pamidronate disodium pwd	30 mg	00083-2601-04		J2430		800-257-3273
Pamidronate disodium pwd	90 mg	00083-2609-01		J2430		800-257-3273
Nipent™						
Pentostatin pwd	10 mg	62701-0800-01		J9268		800-340-8667
Prochlorperazine 5mg/ml, inj	10 ml	00007-3343-01		J0780		800-699-3806
Prochlorperazine 10mg tab	100 tabs	00007-3367-20		Q0165		800-699-3806
Zantac®						
Ranitidine 25mg/ml, inj	2 ml	00173-0362-38		J2780		
Respigam®						
Respiratory Syncytial Virus Immune globul	20 ml	60574-2102-01		J1565		
Respiratory Syncytial Virus Immune globul	50 ml	60574-2101-01		J1565		
Rituxan™						
Rituximab 10mg/ml, inj	10 ml	50242-0051-21		J9310		800-530-3083
Rituximab 10mg/ml, inj	50 ml	50242-0053-06		J9310		800-530-3083
Zanosar®						
Streptozocin, pwd	1 Gm	00009-0844-01		J9320		800-242-7014
Vumon®						
Teniposide 10mg/ml, inj		00015-3075-19		J9999		800-872-8718
Thioplex®						
Thiotepa, pwd		58406-0661-02		J9340		800-321-4669
Hycamtin™						
Topotecan, pwd		00007-4201-01		J9350		800-699-3806
Topotecan, pwd		00007-4201-05		J9350		800-699-3806
Herceptin®						
Trastuzumab, pwd		50242-0134-60		J9355		800-530-3083
Neutrexin®						
Trimetrexate, pwd		58178-0020-10		J3305		800-887-2467
Trimetrexate, pwd		58178-0020-50		J3305		800-887-2467
Trimetrexate, pwd		58178-0021-01		J3305		800-887-2467
Urokinase, pwd		00074-6111-01		J3364		
Urokinase, pwd		00074-6145-02		J3364		
Vinblastine sulfate pwd		55390-0091-10		J9360		
Vinblastine sulfate 1mg/ml, inj		63323-0278-10		J9360		
Vincristine sulfate 1mg/ml, inj		00013-7456-86		J9370		800-242-7014
Vincristine sulfate 1mg/ml, inj		61703-0309-06		J9370		
Vincristine sulfate 1mg/ml, inj		00013-7466-86		J9375		800-242-7014
Vincristine sulfate 1mg/ml, inj		61703-0309-16		J9375		
Navelbine®						
Vinorelbine 10mg/ml, inj		00173-0656-01		J9390		800-423-6869
Vinorelbine 10mg/ml, inj		00173-0656-44		J9390		800-423-6869

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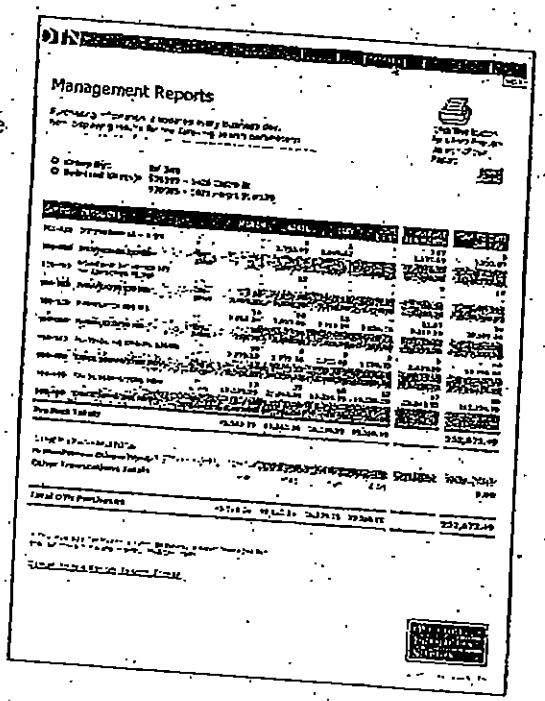

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A Program Supporting the Reimbursement of Oral Chemotherapy and Supportive Care Medicines in Physician Offices

ORCA™

OTN
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An Introduction to ORCA

ORCA (Oral Reimbursement for Cancer Agents) is a free service provided by Oncology Therapeutics Network (OTN), which can simplify and expedite billing and reimbursement for oral chemotherapy and supportive care medicines in your office.*

Why participate?

- Simplifies the use of oral therapies in the physician's office
- Eliminates concerns over reimbursement delays and denials
- Service is provided "free of charge" by OTN

How does ORCA work?

There are four components to the program:

1. Enrollment in the National Supplier Clearinghouse (NSC)
2. Drug fulfillment through OTN
3. Billing, collection, and appeals of individual claims through ORCA
4. Drug replacement is guaranteed if reimbursement is not approved

Which oral medications and insurance carriers are covered by ORCA?

- Cytoxan® Tablets (cyclophosphamide tablets, USP)
- VePesid® (etoposide) Capsules

The ORCA program covers all Medicare patients. It is expected that the program will be expanded in the near future to cover additional chemotherapeutic and supportive care medicines and additional insurance carriers.

Who is eligible to participate in ORCA?

Any office-based physician practice is eligible to participate in the ORCA program.

How do I enroll in the program?

1. If you are not already an OTN customer, call 1-800-482-6700 to set up an account.
2. Once you have set up an account, or if you are already an OTN customer, call the ORCA program at 1-877-SAY-ORCA (1-877-729-6722) to request an enrollment packet.

* The ORCA program is a free service provided by OTN and is administered by AccessMED, 6900 College Boulevard, Suite 1000, Overland Park, KS 66211. AccessMED is a leading reimbursement and consulting firm focused on oncology.

www.melanoma.com

Information about melanoma prevention, diagnosis, and staging

Skin self-examination techniques

Skin safety, sun safety, and risk reduction

Nutrition and exercise tips

Resource listings for melanoma patients, their families, and friends

OTN
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Aventis®

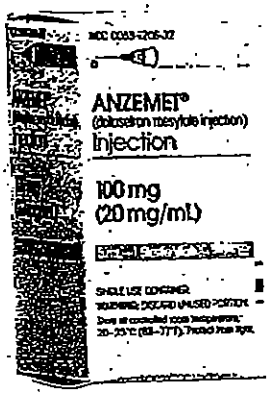
Aventis Pharmaceuticals
Kansas City, MO 64134

J-CODES
Injections: J1260, per 1 mg
Tablets: Q0180, per 100 mg

5-HT$_3$ Receptor Antagonist

Excellent Efficacy and Safety Profile

- **Anzemet Injection** is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin.
- **Anzemet Tablets** are indicated for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy, including initial and repeat courses.
- **Proven Efficacy and Simplicity**— Anzemet injection can be safely infused intravenously as rapidly as 100 mg/30 seconds or diluted in compatible IV solutions and infused over 15 minutes. The recommended oral dosage of Anzemet is 100 mg given within one hour before chemotherapy.



For more information on dosing and administration, please contact your Hoechst Marion Roussel representative.

Great Value!

CATALOG NUMBER	NDC	BRAND NAME	ITEM	UNIT SIZE	ORDER QUANTITY	PRICE/ UNIT	AWP
900-250	0088-1206-32	Anzemet	dolasetron mesylate	100 mg vial	1	$77.75	$155.88
970-300	0088-1203-05	Anzemet	dolasetron mesylate	100 mg tablets	5	$321.45	$343.20
970-305	0088-1203-29	Anzemet	dolasetron mesylate	100 mg tablets blister pack	5	$321.45	$686.40
970-310	0088-1203-43	Anzemet	dolasetron mesylate	100 mg tablets unit dose	10	$642.95	$686.40

Outstanding Support:

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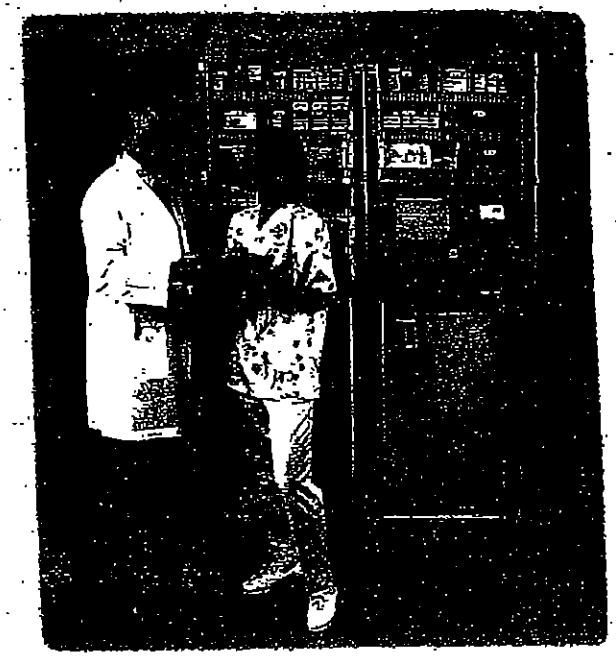

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New Rules Could Affect You

by James Kearney and Barbara Winter-Watson

Over the last several years, industry has developed needles and other sharps injury protection designed to protect workers against exposure to blood and other potentially infectious materials (OPIM). Some surveys suggest that the use of these new safety devices have demonstrated a 23 to 85 percent reduction in needlestick injuries. As a result, the Occupational Safety and Health Administration (OSHA), along with state officials, nursing leaders, and union organizers, are taking steps to publicize the dangers of conventional needles and mandate safer needles in all healthcare settings.

The Risks

According to the Centers for Disease Control and Prevention, healthcare workers in the United States report some 800,000 needlestick injuries each year. Well over half of these reported injuries occur to nurses.

Needlesticks are the most common cause of occupational exposure to HIV, hepatitis B, and hepatitis C. The infection rate from a needlestick involving contaminated blood is about 0.3 percent for HIV, but can reach 10 percent for hepatitis C and 30 percent for hepatitis B.

Research indicates that needlestick injuries often go unreported. According to hospital surveys conducted by several groups, approximately one-third to one-half of all needlesticks go unreported. This could mean that well over 1 million sharps injuries are occurring in the workplace each year (two per minute). Because a single needlestick injury can cost thousands to hundreds of thousands of dollars, the potential cost to the healthcare industry of such injuries can reach hundreds of millions of dollars.

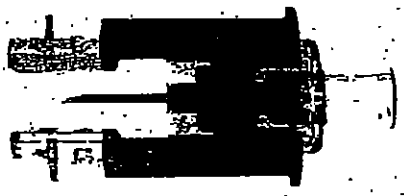
Engineered for Safety

Industry has responded to these significant risks by developing safer needles and needleless systems. Devices such as various retractable and self-sheathing needles are widely available today. "There have been more than 1,000 U.S. patents issued during the past 10 years in the area of safer needle technology," according to Lynda Arnold, RN, founder and president of the grassroots organization National Campaign for Healthcare Worker Safety, whose mission is to get every U.S. hospital to agree to replace conventional blood drawing needles and IV catheters with the newer safety devices.

Unfortunately, many of these safety devices are not making it to the healthcare setting. There are a lot of pressures on industry to maintain costs, and because the Food and Drug Administration (FDA) has not banned conventional needles, these costs are the major factor preventing hospitals from purchasing these new safety devices. Manufacturers themselves also have little financial incentive to publicize the availability of these safety devices because upwards of 90 percent of their sales are from conventional devices.

New Mandates

Needlestick safety devices are now the law in five states—California, Texas, Tennessee, Maryland and New Jersey—and similar legislation is pending in some 16 others. For example, California OSHA has put into place stronger requirements for employers to use needles and other sharps that are engineered to reduce the chances of inadvertent needlesticks or sharps injuries. They now mandate the use of "needleless systems, needle devices with engineered sharps injury protection, and non-needle sharps with engineered sharps injury protection." In an effort to increase reporting of workplace needlesticks, California also now requires a sharps injury log be kept, which records the date and time of each sharps injury resulting in an exposure incident, as well as the brand of device involved.



Federal OSHA has recently changed its enforcement guidance on the federal Bloodborne Pathogens standard (29 CFR 1910.1030) as a means to encourage companies to use the newer devices. Essentially, OSHA now considers safe needle technology to have advanced to the point where its effectiveness and availability make it justifiable to require their use in health care settings. *http://www.osha-slc.gov/OshDoc/Directive_data/CPL_2-2_44D.html#CLARIFICATION*

OSHA considers safe needles and needleless devices to be "engineering controls," and issues this warning in its Guidance:

"NOTE: Where engineering controls will reduce employee exposure either by removing, eliminating or isolating the hazard, they must be used. Significant improvements in technology are most evident in the growing market of safer medical devices that minimize, control or prevent exposure incidents."

Paragraph (d)(2)(i) requires the employer to institute engineering and

See NEEDLESTICK, page 10

ONCOLOGY DRUG UPDATES

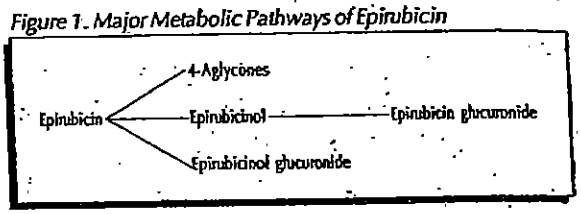
Epirubicin for the Adjuvant Treatment of Node-Positive Breast Cancer: A Comparison with Doxorubicin

by Claire E. Gilmore PharmD, BCOP

In the Fall of 1999, after a unanimous recommendation by the members of the Oncologic Drugs Advisory Committee of the Food and Drug Administration (FDA), epirubicin hydrochloride (Ellence®, Pharmacia) became the first cytotoxic agent approved as a component of adjuvant therapy for women with axillary lymph-node–positive breast cancer. Epirubicin, the 4'-epimer of doxorubicin, is an anthracycline cytotoxic agent that has been marketed worldwide since 1982 for the treatment of several cancers, including breast, ovarian, lung, stomach, liver, and bladder; lymphomas; and sarcomas.[1]

Currently, several different combination chemotherapy regimens are used as adjuvant therapy of node-positive early breast cancer. Excluding epirubicin-containing regimens, these regimens include doxorubicin and cyclophosphamide (AC); cyclophosphamide, methotrexate, and fluorouracil (CMF); cyclophosphamide, doxorubicin, and fluorouracil (CAF); and AC followed by paclitaxel. Recently, the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) published results of a meta-analysis of polychemotherapy of early breast cancer, which compared anthracycline-containing regimens (both doxorubicin and epirubicin) with CMF as adjuvant therapy of early breast cancer.[2] Results of this analysis demonstrated a superiority of anthracycline-containing regimens over CMF in both reducing breast cancer recurrence rates (12% proportional risk reduction; P=.006) and improving mortality (11% proportional risk reduction, P=.02).

Figure 1. Major Metabolic Pathways of Epirubicin



Epirubicin versus Doxorubicin

Pharmacologic and Pharmacokinetic Differences

The proposed mechanism of cytotoxic activity of epirubicin includes DNA intercalation, which inhibits DNA, RNA, and protein synthesis and triggers DNA cleavage by topoisomerase II.[3,4] Although epirubicin and doxorubicin vary only by the orientation of the 4'-hydroxyl group (equatorial in epirubicin and axial in doxorubicin), clinically significant pharmacologic differences exist. First, epirubicin has a lower pKa than does doxorubicin, which makes it more lipophilic and better able to penetrate cell membranes.[5] Second, unlike doxorubicin, epirubicin undergoes glucuronidation in the liver into inactive metabolites (Figure 1). Because of this rapid plasma clearance, epirubicin has a shorter half-life than that of doxorubicin (approximately 30 vs 45 hours), which reduces patient exposure to metabolites that are potentially toxic to normal tissues, including the heart.[5]

Differences in Toxicity

The toxicity profile of epirubicin is more favorable than that of doxorubicin. Clinical trials comparing equimolar doses of epirubicin and

NEEDLESTICK, CONTINUED

work practice controls as the primary means of eliminating or minimizing employee exposure. OSHA has also required employers to use engineering and work practice controls, but safer needle devices were not readily available when the standard was first put out in 1991. Thus the employer is expected to implement work practice controls that eliminate or minimize exposure to the lowest feasible extent. Evaluating exposures requires a comprehensive review of existing controls (e.g., needleless devices, sharps containers, capillary tubes) and proper work practices (e.g., handling contaminated sharps, passing in the operating room).

It appears that momentum is building for the use of engineered needlestick injury prevention devices in clinical settings. Although these devices will not prevent all needlesticks and other sharps injuries, it is likely that they will contribute to a significant reduction in both injuries and costs to industry.

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AN UPDATE FOR COMMUNITY-BASED ONCOLOGY PROFESSIONALS

Extra

Glutamine and Cancer Therapy Symptom Management

by Melodie Thomas, BSN, RN, OCN, CCRP
Director of Research Nursing
The Sarah Cannon Cancer Center, Nashville, TN

Introduction

Patients with cancer receiving chemotherapeutic agents must cope with a wide range of therapy-induced symptoms that are often difficult for physicians and nurse clinicians to manage. Recent data suggests a potential benefit of supplementation with the amino acid glutamine during chemotherapy to prevent and treat various toxicities, including mucositis, arthralgia, myalgia, diarrhea and peripheral neuropathy. The purpose of this article is to educate the oncology nurse on the current status and potential role of glutamine in successfully managing these treatment-associated toxicities.

The Role of Glutamine

Of the 20 amino acids involved in protein synthesis, glutamine is the most abundant. It is found in blood and tissues[1], and is primarily formed and stored in skeletal muscle and the lungs.[2] Some of the functions of glutamine in the body include: (1) donating nitrogen for various synthetic pathways; (2) serving as a precursor in both nucleic acid and nucleotide synthesis; (3) playing a role in acid-base balance in the body; (4) serving as a precursor of neurotransmitters; and (5) providing an energy source for cells of the immune system, specifically lymphocytes and macrophages.[3] Glutamine also plays a role as a regulator of glycogen synthesis and is an important metabolic substrate for cells of the intestinal mucosa.[4] Glutamine has classically been considered a nonessential amino acid, as it is synthesized by the body rather than having to be obtained solely through the diet. However, when the body experiences metabolic stress or catabolic disease states, glutamine deficiency can occur following the free release of glutamine from skeletal muscle which causes intracellular glutamine concentrations to drop by 50% or more. This observation has led to the more recent classification of glutamine as a conditionally essential amino acid.[4-6] The importance of glutamine in the body would seem to argue for the inclusion of glutamine to any form of nutritional support given to a patient experiencing metabolic stress, regardless of the underlying cause.

The Role of Glutamine in Tumors

Cancer is among the disease states that can lead to depletion of glutamine from the body.[7] Because glutamine is a primary source of energy for rapidly growing tumors, tumors are often referred to as glutamine traps. In cases of advanced malignant disease, glutamine depletion from skeletal muscle can be quite serious, leading to cachexia. There was understandably some hesitation at the idea of supplementing the cachexic cancer patient with glutamine due to concerns that this could stimulate tumor growth. However, as studies examining the effect of supplemental glutamine on tumor growth have been completed, it has emerged that there is no enhancement of tumor growth with glutamine supplementation. In fact, recent studies have suggested evidence that glutamine supplementation may decrease tumor growth.[8-10]

Proposed mechanisms by which glutamine supplementation decreases tumor growth include up-regulation of the immune system increasing susceptibility of tumor cells to chemotherapy. Results from a variety of studies conducted using animal models suggest that glutamine up-regulates the immune system by increasing the activity of the subset of T-cells known as natural killer cells.[11-14] Glutamine also appears to exert an effect via changes in glutathione metabolism. Rouse, et al. demonstrated that rats receiving glutamine had decreased glutathione levels in tumor tissue which corresponded to increased susceptibility to chemotherapy, while glutathione levels in normal tissue were

Continued on next page

increased or maintained, helping to protect the cells from injury.[15] Therefore, glutamine may serve to simultaneously protect normal tissues from chemotherapy and increase susceptibility of the tumor cells.

Glutamine and Cancer Therapy Symptom Management

During the past decade, glutamine has been studied extensively in both animal and human clinical trials. Human trials demonstrate glutamine is safe to deliver with a variety of chemotherapeutic agents with no added toxicity.[16,17] In addition, randomized human trials have been performed that show glutamine supplementation can significantly reduce the duration and severity of chemotherapy associated stomatitis.[16,17] Savarese et al. published a case report involving five patients treated with glutamine for the management of paclitaxel-induced arthralgia and myalgia.[18] The patients received paclitaxel 175mg/m^2 - 200mg/m^2, over 1 to 3 hours, either alone or in combination. All patients developed moderate to severe myalgia and/or arthralgia within 24-36 hours after the initial course of treatment. After the second treatment, the patients received glutamine 10 grams by mouth, three times daily, beginning 24 hours after the paclitaxel dose. None of the five patients developed myalgia or arthralgia while receiving the glutamine.

Animal data demonstrate oral glutamine can be delivered during radiation therapy and assist in maintaining the gut mucosal barrier and integrity of enterocytes. Boyle, et al. used a rat model to explore the effects of glutamine supplementation on peripheral neuropathy associated with vincristine[19] and with paclitaxel and cisplatin[20]. The authors concluded that glutamate (the acid of glutamine) appears to be an effective neuroprotectant, against both sensory and motor neuropathy, without compromising the anti-tumor activity of paclitaxel. Although the mechanism of neuroprotection by glutamine was not elucidated, this work prompted clinical trials involving glutamine supplementation in humans.

Summary

In conclusion, data in both animals and humans support dietary supplementation with oral glutamine for the management of chemotherapy and radiation therapy induced toxicities. Clinical trials are currently underway in NCI-sponsored Cooperative Groups as well as academic and hospital-based cancer centers further evaluating the role of glutamine for management of therapy induced mucositis, diarrhea, arthralgia, myalgia and neuropathy. Although trials are underway, the optimal dose and schedule of glutamine has not yet been determined in cancer patients. However, anecdotal experiences utilizing 10 grams of glutamine powder three times daily beginning the day of chemotherapy or 24 hours following for three to five days has resulted in significant symptom reduction. The role of the oncology nurse is vital in the effective management of treatment-related toxicities. Early symptom assessment and utilization of oral glutamine may significantly reduce these toxicities and enhance quality of life for patients with cancer.

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doxorubicin have established the following doxorubicin-to-epirubicin dose ratios that produce similar degrees of toxicity: hematologic, 1:1.2; nonhematologic, 1:1.5; and cardiac, 1:1.8.[3] The primary acute toxicities of epirubicin include a reversible neutropenia, mucositis, nausea and vomiting, and alopecia.[3] Cardiotoxicity, typically manifested as congestive heart failure (CHF), may also occur following epirubicin administration.[3] However, the probability of developing CHF with epirubicin occurs at approximately twice the cumulative dose of doxorubicin—between 950 and 1,000 mg/m² of epirubicin compared with 450 mg/m² of doxorubicin.[6,7] Secondary acute myelogenous leukemia (AML) has also been reported following treatment with epirubicin or doxorubicin in a cyclophosphamide-containing combination regimen, but the incidence is rare with either (less than 1% at 5 years for epirubicin and less than 1% at 4 years for doxorubicin).[8,8] Secondary AML has been reported in patients treated with topoisomerase II inhibitors, including anthracyclines, and occurs more commonly when these drugs are combined with DNA-damaging cytotoxic agents, such as cyclophosphamide.

Evidence suggests that both epirubicin and doxorubicin display a steep dose-response relationship in breast cancer treatment. However, because of toxicities, including cardiotoxicity, mucositis, and hand-foot syndrome, doxorubicin doses cannot be escalated in single doses greater than 75 to 100 mg/m², whereas epirubicin can be administered in single doses as high as 180 mg/m².[9,10]

Clinical Trials of Epirubicin and Doxorubicin in the Adjuvant Treatment of Early Breast Cancer

Anthracycline-based regimens are gaining in popularity over CMF as adjuvant therapy of women with node-positive early breast cancer based on encouraging clinical trial data coupled with favorable results of the EBCTCG meta-analysis, the National Comprehensive Cancer Network practice guidelines, and recommendations from the St. Gallen International Consensus Panel.[2,11,12] Results of 2 large randomized trials of women with node-positive breast cancer demonstrated no difference in overall survival (OS) times between 4 cycles of AC and 6 cycles of CMF or 6 cycles of CAF and 6 cycles of CMF (Table 1).[13,14] Only 1 trial has documented the superiority of a doxorubicin-based regimen over CMF in both disease-free survival (DFS) and OS times; however, this Oncofrance trial compared 12 cycles of treatment with doxorubicin, vincristine, cyclophosphamide, and fluorouracil (AVCF) with CMF (Table 1), which is an impractical approach because most chemotherapy regimens for advanced breast cancer are administered over only 4 to 6 cycles.[15] A US Intergroup trial compared CAF with CMF; CAF demonstrated a marginally superior survival time but was more toxic than CMF.[16] Of note, only high-risk patients with node-negative early breast cancer were included.

Epirubicin was FDA approved as adjuvant therapy of early breast cancer based on data from 2 large, phase III randomized trials—a pivotal trial sponsored by the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG) reported by Levine et al[17] and a supportive trial sponsored by the French Adjuvant Study Group (FASG) reported by Bonneterre et al (Table 1).[18] The NCIC CTG MA.5 trial compared dose-intensive cyclophosphamide, epirubicin, and fluorouracil (CEF) with CMF in

Continued on next page

Table 1. Trials of Adjuvant Doxorubicin- or Epirubicin-Containing Regimens vs CMF

Study	Patient Population	No. of Patients	Regimen	Relapse-Free Survival Rate	Overall Survival Rate
EBCTCG[2]	All	5,942	Anthracycline-containing regimen vs CMF	57.3% vs 54.1% (P=.006)	63.8% vs 63.8% (P=.02)
Fisher et al[13]	Node-positive	2,194	[illegible]	DFS: 62% vs 63% (P=NS)	[illegible] vs 62% (P=NS)
Carpenter et al[14]	Node-positive	528	[illegible] vs CMF	NR	[illegible] vs 68% (P=NS)
Misset et al[15]	Node-positive	249	AVCF vs CMF	DFS: 53% vs 36% (P=.006)	[illegible] vs 41% (P=.04)
Hutchins et al[16]	Node-negative	2,691	CAF vs CMF	DFS: 85% vs 82% (P=.03)	[illegible]
Levine et al[17]	Node-positive	710	[illegible]	63% vs 53% (P=.009)	[illegible]
Bonneterre et al[18]	Node-positive	565	FEC [illegible] vs FEC [illegible]	65% vs 52% (P=.007)	[illegible]
Wils et al[20]	Node-positive	604	Epirubicin [illegible] vs [illegible]	73.7% vs 62.1% (P=.023)	[illegible] vs 77.0% (P=NS)
Mouridsen et al[19]	All	1,195	CEF vs CMF	63% vs 58% (P=.003)	[illegible] vs 65% (P=.009)

A=doxorubicin; C=cyclophosphamide; DFS=disease-free survival; E=epirubicin; F=fluorouracil; M=methotrexate; NR=not reported; NS=not significant; P=prednisone; V=vincristine

710 pre- or perimenopausal women with node-positive breast cancer (Table 2).[17] With 5 years of follow-up, both relapse-free survival (RFS) and OS times were statistically significantly prolonged in the CEF group compared with the CMF group. Of note, this trial and the Oncofrance trial of 12 cycles of AVCF vs CMF were the 2 studies in the EBCTCG overview analysis that documented a clear superiority of anthracycline-based regimens over CMF.[2,15,17] Bonneterre et al[18] randomized 565 women with node-positive breast cancer to receive 6 cycles of fluorouracil, epirubicin (100 mg/m² or 50 mg/m²), and cyclophosphamide (FEC 100 or FEC 50) (Table 2). With a median follow-up of 5 years, both RFS and OS times were statistically significantly prolonged in the FEC 100 group compared with the FEC 50 group, thereby demonstrating a clear dose-response effect for epirubicin-based adjuvant therapy.

Table 2. Adjuvant Epirubicin-Containing Regimens

	Levine et al[20]	Bonneterre et al[18]
Treatment arm	CEF 120 q 4 wk	FEC 100 q 3 wk
	C 75 mg/m² po days 1–14 E 60 mg/m² IV days 1 + 8 F 500 mg/m² IV days 1 + 8	F 500 mg/m² IV day 1 E 100 mg/m² IV day 1 C 500 mg/m² IV day 1
Control arm	CMF q 4 wk	FEC 50 q 3 wk
	C 100 mg/m² po days 1–14 M 40 mg/m² IV days 1 + 8 F 600 mg/m² IV days 1 + 8	F 500 mg/m² IV day 1 E 50 mg/m² IV day 1 C 500 mg/m² IV day 1

C=cyclophosphamide; E=epirubicin; F=fluorouracil; M=methotrexate.

The results of 2 additional phase III studies strongly support the use of epirubicin in the adjuvant treatment of early breast cancer.[19,20] Wils et al[19] reported results of a trial sponsored by the International Collaborative Cancer Group in which 604 postmenopausal women with node-positive, operable breast cancer were randomly assigned to receive adjuvant therapy with prolonged tamoxifen therapy alone or in combination with single-agent epirubicin (50 mg/m² days 1 and 8). Epirubicin plus tamoxifen produced a 28% reduction (P=.023) in the odds of breast cancer recurrence and a 12% reduction in mortality compared with tamoxifen alone, making this the first study to document an improvement in RFS with single-agent adjuvant chemotherapy. In a trial sponsored by the Danish Breast Cancer Cooperative Group and reported by Mouridsen et al,[20] 1,195 high-risk breast cancer patients (both pre- and postmenopausal, both node-positive and node-negative) were randomized to receive CEF or CMF. A statistically significant difference in RFS and OS times was observed in the combined analysis of the 3 subgroups of CEF compared with CMF.

Pharmaceutical and Clinical Practice Issues

The recommended starting dose of epirubicin as a component of adjuvant therapy with fluorouracil and cyclophosphamide is 100 mg/m² on day 1 of each 3-week cycle or 60 mg/m² on days 1 and 8 of each 4-week cycle. Epirubicin is available in 2 single-use vial sizes—50 mg and 200 mg—that should be refrigerated while unopened and used within 24 hours of the first penetration of the rubber stopper. As a precaution against infections, patients who receive the 120-mg/m² (60 mg/m²) dose should also receive prophylactic antibiotic therapy with trimethoprim-sulfamethoxazole or a fluoroquinolone. This recommendation is based on the results of a pilot study showing antibiotic prophylaxis reduced the risk of febrile neutropenia in patients receiving epirubicin 120 mg/m².[21] Standard dose modifications exist for hematologic and nonhematologic toxicities. Because epirubicin is eliminated by hepatic metabolism and biliary excretion, dose reductions are recommended for patients with hepatic dysfunction.

Conclusions

It is apparent that adjuvant regimens containing epirubicin are associated with a significant prolongation in RFS and OS times compared with standard therapies, such as CMF. As expected with any anthracycline agent, epirubicin is associated with cardiotoxicity; however, when epirubicin is compared with doxorubicin at equimolar doses, the incidence of cardiotoxicity is much lower with epirubicin. Furthermore, dose-intensification with epirubicin is feasible and well tolerated, resulting in improved outcomes not observed with doxorubicin. Positive effects of epirubicin-containing regimens have been observed across a range of subgroups, including patients with node-positive or node-negative disease, premenopausal and postmenopausal patients, and patients with hormone-receptor–positive and –negative tumors. Ongoing research efforts are focusing on combining anthracyclines with newer cytotoxic agents, such as the taxanes, as a

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method to improve outcomes following adjuvant therapy. Doxorubicin-taxane combinations have shown excellent antitumor activity, but at the expense of an unfavorable cardiotoxicity profile.[22,23] Epirubicin-taxane combinations are highly active and appear to be well tolerated, thus setting the stage for further research of this combination as adjuvant therapy.[24,25] With its favorable clinical activity and side effect profile, epirubicin is challenging doxorubicin as the anthracycline of choice for the adjuvant treatment of early breast cancer.

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BP 01289

ONCOLOGY THERAPEUTICS NETWORK

ODAC RECOMMENDATIONS

The Food and Drug Administration's (FDA's) Oncologic Drugs Advisory Committee (ODAC) met in March 2000 to review data for 3 drugs. Gemtuzumab ozogamicin (Mylotarg®, Wyeth-Ayerst Laboratories) received accelerated approval for the treatment of patients 60 years of age or older with CD33-positive relapsed acute myeloid leukemia (AML). Gemtuzumab is a humanized recombinant monoclonal antibody that is specific for the CD33 antigen, which is commonly expressed by myeloid leukemia cells. In clinical trials, gemtuzumab 9 mg/m² was administered as a 2-hour intravenous (IV) infusion on days 1 and 15.[1] The primary nonhematologic side effect of gemtuzumab is self-limited fever and chills, which requires premedication with diphenhydramine and acetaminophen; hyperbilirubinemia and hepatic transaminase elevations may also occur. Neutropenia and thrombocytopenia are the primary hematologic toxicities. Of note, gemtuzumab lessened mucositis and length of hospitalization.

Irinotecan (Camptosar®, Pharmacia & Upjohn) has received unanimous approval for an expanded indication as a first-line therapy, in combination with 5-fluorouracil (5-FU) and leucovorin, for metastatic colorectal cancer (MCRC). Irinotecan had previously received FDA approval as second-line therapy of MCRC. Data supporting this indication came from 2 pivotal phase III trials, in which irinotecan increased overall survival times.[2,3] In a US study, 231 patients with MCRC received irinotecan 125 mg/m² IV over 90 minutes followed by leucovorin 20 mg/m² and 5-FU 500 mg/m² (both IV bolus) weekly for 4 weeks, with this regimen repeated every 6 weeks.[2] The control groups received a standard 5-FU-leucovorin regimen (n=226) or single-agent irinotecan (n=226). The median survival time was significantly prolonged in the irinotecan combination group compared with the 5-FU-leucovorin group (14.8 vs 12.6 months, $P=.042$). Additionally, time to tumor progression was significantly prolonged in the irinotecan combination group compared with the 5-FU-leucovorin group (7 vs 4.3 months, $P=.0041$). In a European study, the median survival time was significantly prolonged for 198 patients who received irinotecan plus 5-FU-leucovorin compared with 187 patients who received 5-FU-leucovorin alone (17.4 months vs 14.1 months, $P=.032$).[3] Primary side effects of irinotecan include delayed diarrhea, neutropenia, alopecia, nausea and vomiting, cholinergic symptoms, anorexia, and asthenia.

A third drug reviewed by the ODAC in March, oxaliplatin (Eloxatine®, Sanofi Synthelabo), did not receive approval as first-line therapy for patients with MCRC. Concerns about increased neurotoxicity and lack of improved survival rates were potential reasons why this new drug application was not approved.

Recent FDA Approvals Anticancer Drugs

The FDA approved several new agents in March. Leuprolide acetate implant (Viadur®, Alza Corporation) was approved as an annual palliative treatment for advanced prostate cancer. Leuprolide acetate implant is a miniature titanium cylinder that provides continuous delivery of stable drug for 12 months. Common side effects in clinical trials of leuprolide acetate implant included vasodilation (hot flashes), asthenia, gynecomastia, and bruising at the insertion site. Leuprolide acetate implant also causes a transient increase in serum testosterone levels during the first week of treatment, which may result in worsening of symptoms, particularly pain or bladder outlet obstruction symptoms.

Pacis BCG® (Bacillus Calmette-Guérin [BCG], BioChem Pharma Inc) intravesical immunotherapy, which contains live, attenuated BCG mycobacteria, received FDA approval for the treatment of carcinoma in situ of the urinary bladder. The recommended course of treatment is a weekly outpatient dose for 6 weeks.

Anticancer Orphan Drug Products

The Office of Orphan Products Development of the FDA has recently granted orphan drug designation to several drugs, including Pentacea® (IBC Pharmaceuticals) for the treatment of small cell lung cancer. Pentacea is a form of tumor-targeted radiation therapy. Histamine dihydrochloride (Maxamine®, Maxim Pharmaceuticals) has been granted orphan drug status as an adjunct to cytokine therapy for the treatment of acute myeloid leukemia and malignant melanoma. Thymalfasin (Zadaxin®, SciClone Pharmaceuticals) was also granted orphan status as immunotherapy for the treatment of hepatocellular carcinoma.

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- [redacted] based on your AREDIA unit purchases [redacted] participants will be eligible to receive [redacted] 4% or 5% depending on the growth [redacted] purchases during the year 2000 [redacted] the year 1999.
- [redacted] if you achieve an increase up to 10% over your total 1999 AREDIA milligram purchases
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- [redacted] if you achieve an increase >20% over your total 1999 AREDIA milligram purchases

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January 2000

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REIMBURSEMENT

ONCOLOGY THERAPEUTICS NETWORK

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Anzemet®						
Dolasetron 20mg/ml, inj	5 ml	00088-1206-32	155.88	J1260	10mg	800-221-4025
Rubex®						
Doxorubicin HCl, pwd	50 mg	00015-3352-22	197.15	J9000	10mg	800-872-8718
Doxorubicin HCl, pwd	100 mg	00015-3353-22	394.29	J9000	10mg	800-872-8718
Doxorubicin HCl, pwd	10 mg	55390-0231-10	45.08	J9000	10mg	
Doxorubicin HCl, pwd	20 mg	55390-0232-10	90.16	J9000	10mg	
Doxorubicin HCl, pwd	50 mg	55390-0233-01	225.40	J9000	10mg	
Doxorubicin HCl 2mg/ml, inj	5 ml	55390-0235-10	47.35	J9000	10mg	
Doxorubicin HCl 2mg/ml, inj	10 ml	55390-0236-10	94.70	J9000	10mg	
Doxorubicin HCl 2mg/ml, inj	25 ml	55390-0237-01	236.74	J9000	10mg	
Doxorubicin HCl 2mg/ml, inj	100 ml	55390-0238-01	945.98	J9000	10mg	
Adriamycin®						
Doxorubicin RDF, pwd	10 mg	00013-1086-91	53.64	J9000	10mg	800-242-7014
Doxorubicin RDF, pwd	50 mg	00013-1106-79	268.18	J9000	10mg	800-242-7014
Doxorubicin RDF, pwd	150 mg	00013-1116-83	788.44	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml, inj	5 ml	00013-1136-91	56.34	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml	10 ml	00013-1146-91	112.66	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml	25 ml	00013-1156-79	281.68	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml	37.5 ml	00013-1176-87	422.51	J9000	10mg	800-242-7014
Doxorubicin HCl pfs 2mg/ml	100 ml	00013-1166-83	1,104.13	J9000	10mg	800-242-7014
Doxil®						
Doxorubicin, HCL liposome 2mg/ml inj	10 ml	61471-0295-12	656.25	J9001	10mg	800-609-1082
Procrit®						
Epoetin Alpha 2000u/ml inj	1 ml	59676-0302-01	24.00	Q0136	1,000units	800-553-3851
Epoetin Alpha 3000u/ml inj	1 ml	59676-0303-01	36.00	Q0136	1,000units	800-553-3851
Epoetin Alpha 4000u/ml inj	1 ml	59676-0304-01	48.00	Q0136	1,000units	800-553-3851
Epoetin Alpha 10, 000u/ml inj	1 ml	59676-0310-01	120.00	Q0136	1,000units	800-553-3851
Epoetin Alpha 20, 000u/ml inj	1 ml	59676-0320-01	240.00	Q0136	1,000units	800-553-3851
Epoetin Alpha 40, 000u/ml inj	1 ml	59676-0340-01	480.00	Q0136	1,000units	800-553-3851
VePesid®						
Etoposide 50mg Capsule	20 caps	00015-3091-45	967.34	J8560	50mg	800-872-8718
Etoposide 20mg/ml, inj	5 ml	00015-3095-20	136.49	J9182	100mg	800-872-8718
Etoposide 20mg/ml, inj	7.5 ml	00015-3084-20	204.74	J9182	100mg	800-872-8718
Etoposide 20mg/ml, inj	25 ml	00015-3061-20	665.38	J9182	100mg	800-872-8718
Etoposide 20mg/ml, inj	50 ml	00015-3062-20	1,296.64	J9182	100mg	800-872-8718
Etopophos®						
Etoposide Phosphate, pwd	100 mg	00015-3404-20	124.14	J9182	100mg	800-872-8718
Fludara®						
Fludarabine Phosphate, pwd	50 mg	50419-0511-06	242.25	J9185	50mg	800-473-5832
Fluorouracil 50mg/ml, inj	10 ml	00013-1036-91	3.20	J9190	500mg	800-242-7014
Fluorouracil 50mg/ml, inj	50 ml	00013-1046-94	16.04	J9190	500mg	800-242-7014
Fluorouracil 50mg/ml, inj	100 ml	00013-1056-94	32.06	J9190	500mg	800-242-7014
Neupogen®						
Filgrastim(G-CSF) 300mcg/ml, inj	300 mcg	55513-0530-10	172.30	J1440	300mcg	800-272-9376
Filgrastim(G-CSF) 300mcg/ml, inj	480 mcg	55513-0546-10	274.40	J1441	480mcg	800-272-9376
Gemzar®						
Gemcitabine HCl, pwd	200 mg	00002-7501-01	93.12	J9201	200mg	888-443-6927
Gemcitabine HCl, pwd	1 Gram	00002-7502-01	465.59	J9201	200mg	888-443-6937
Leukine®						
Sargramostim(GM-CSF), pwd	250 mcg	58406-0002-33	144.30	J2820	50mcg	800-321-4669
Sargramostim(GM-CSF) 500mcg/ml, Inj	1 ml	58406-0050-30	288.59	J2820	50mcg	800-321-4669
Zoladex®						
Goserelin Acetate, implant	3.6 mg syringe	00310-0960-36	469.99	J9202	3.6mg	800-400-4140
Goserelin Acetate, implant	10.8 mg syringe	00310-0961-30	1,409.96	J9202	3.6mg	800-400-4140
Kytril®						
Granisetron HCl 1mg/ml, inj	1 ml	00029-4149-01	195.20	J1626	100mcg	800-699-3806
Granisetron HCl 1mg/ml, inj	4 ml	00029-4152-01	780.80	J1626	100mcg	800-699-3806
Ifex®						
Ifosfamide pwd	1 Gram	00015-0556-41	148.85	J9208	1gm	800-872-8718
Ifosfamide pwd	3 Gram	00015-0557-41	446.55	J9208	1gm	800-872-8718
Ifex®/Mesnex™						
Ifosfamide(10x1g)/Mesna(10x1g MDV)	Combo-Pack	00015-3554-27	2,474.09	J9208/J9209	1gm/200mg	800-872-8718
Ifosfamide(2x3g)/Mesna(6x1g MDV)	Combo-Pack	00015-3564-15	1,484.39	J9208/J9209	1gm/200mg	800-872-8718
Ifosfamide(5x1g)/Mesna(3x1g MDV)	Combo-Pack	00015-3556-26	1,023.90	J9208/J9209	1gm/200mg	800-872-8718
Venoglobulin S						
Immune Globulin 50mg/ml, inj w/IV set	50 ml	49669-1612-01	225.00	J1561	500mg	
Immune Globulin 50mg/ml, inj w/IV set	100 ml	49669-1613-01	450.00	J1561	500mg	